Connecting via Winsock to STN

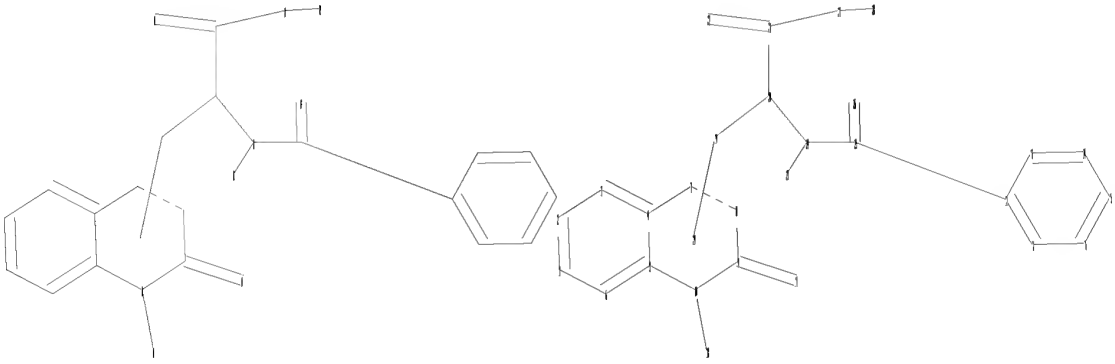
Welcome to STN International! Enter x:x

* * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:21:10 ON 23 JUL 2009

=>
=> file reg

=>
Uploading C:\Program Files\Stnexp\Queries\10586453.str



chain nodes :
17 18 19 20 21 22 23 24 25 26 27 28 30
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
chain bonds :
9-17 10-18 12-25 19-20 20-21 20-24 21-22 21-23 23-28 24-25 24-27 25-26
ring bonds :
1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-10 7-8 8-9 9-10 11-12 11-16 12-13 13-14
14-15 15-16
exact/norm bonds :
4-7 5-10 7-8 8-9 9-10 9-17 20-24 24-25 25-26

```
exact bonds :
10-18  12-25  19-20  20-21  23-28  24-27
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6  11-12  11-16  12-13  13-14  14-15  15-16  21-22
21-23
isolated ring systems :
containing 1 : 11 :


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  16:Atom  17:CLASS  18:CLASS  19:CLASS
20:CLASS  21:CLASS  22:CLASS  23:CLASS  24:CLASS  25:CLASS  26:CLASS  27:CLASS
28:CLASS  29:Atom  30:CLASS



L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l1 sam
SAMPLE SEARCH INITIATED 12:21:40 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      509 TO ITERATE

100.0% PROCESSED      509 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         8827 TO    11533
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 12:21:44 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    10021 TO ITERATE

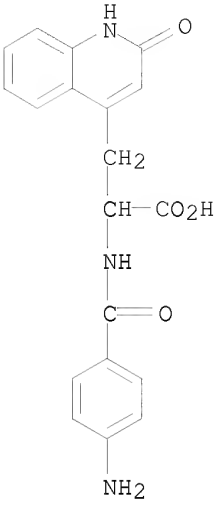
100.0% PROCESSED    10021 ITERATIONS                                3 ANSWERS
SEARCH TIME: 00.00.01

L3            3 SEA SSS FUL L1

=> d scan

L3   3 ANSWERS   REGISTRY  COPYRIGHT 2009 ACS on STN
IN   4-Quinolinepropanoic acid, α-[(4-aminobenzoyl)amino]-1,2-dihydro-2-
     oxo-
```

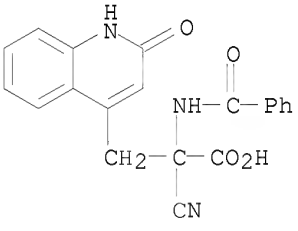
MF C19 H17 N3 O4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

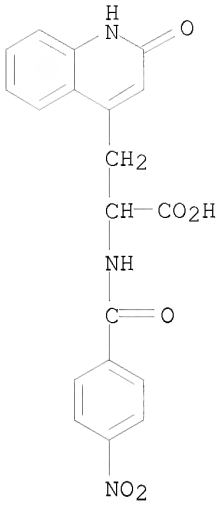
L3 3 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN 4-Quinolinepropanoic acid, α-(benzoylamino)-α-cyano-1,2-dihydro-2-oxo-
MF C20 H15 N3 O4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

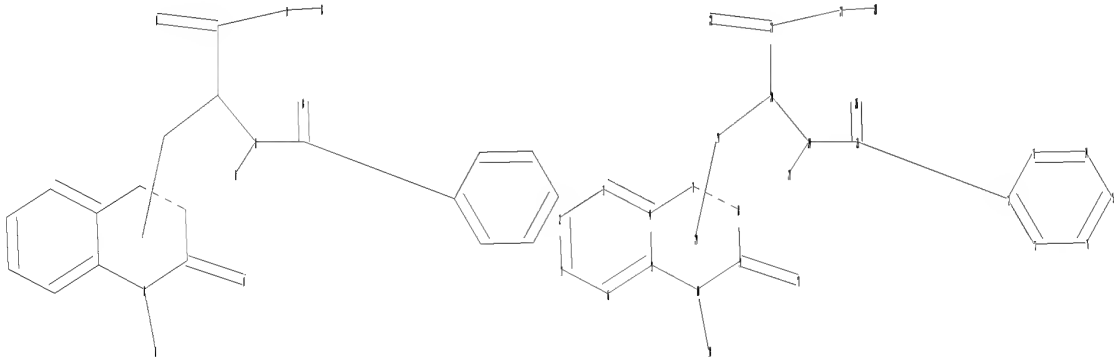
L3 3 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN 4-Quinolinepropanoic acid, 1,2-dihydro-α-[(4-nitrobenzoyl)amino]-2-oxo-
MF C19 H15 N3 O6



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=>
Uploading C:\Program Files\Stnexp\Queries\20586453.str



chain nodes :

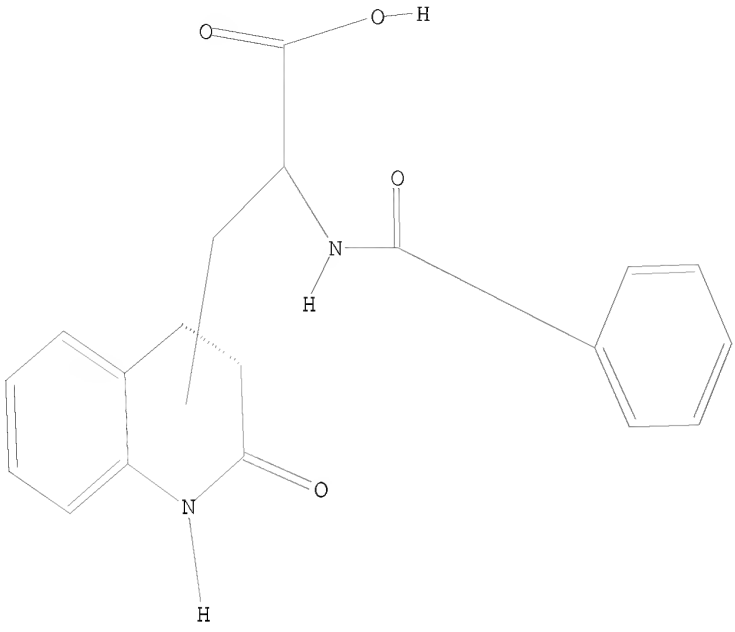
```
17  18  19  20  21  22  23  24  25  26  27  28
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16
chain bonds :
9-17  10-18  12-25  19-20  20-21  20-24  21-22  21-23  23-28  24-25  24-27  25-26
ring bonds :
1-2  1-6  2-3  3-4  4-5  4-7  5-6  5-10  7-8  8-9  9-10  11-12  11-16  12-13  13-14
 14-15  15-16
exact/norm bonds :
4-7  5-10  7-8  8-9  9-10  9-17  20-24  24-25  25-26
exact bonds :
10-18  12-25  19-20  20-21  23-28  24-27
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6  11-12  11-16  12-13  13-14  14-15  15-16  21-22
21-23
isolated ring systems :
containing 1 : 11 :


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  16:Atom  17:CLASS  18:CLASS  19:CLASS
20:CLASS  21:CLASS  22:CLASS  23:CLASS  24:CLASS  25:CLASS  26:CLASS  27:CLASS
28:CLASS  29:Atom



L4      STRUCTURE UPLOADED

=> d l4
L4 HAS NO ANSWERS
L4              STR
```



Structure attributes must be viewed using STN Express query preparation.

```
=> s l4 sam
SAMPLE SEARCH INITIATED 12:22:49 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      509 TO ITERATE

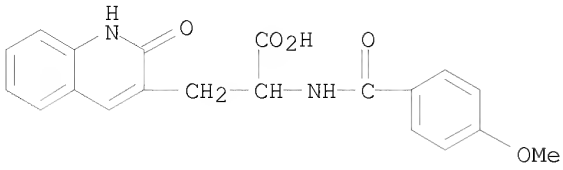
100.0% PROCESSED      509 ITERATIONS                                3 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         8827 TO    11533
PROJECTED ANSWERS:               3 TO      163

L5            3 SEA SSS SAM L4

=> d scan

L5   3 ANSWERS   REGISTRY  COPYRIGHT 2009 ACS on STN
IN   3-Quinolinepropanoic acid, 1,2-dihydro-α-[(4-methoxybenzoyl)amino]-2-
     oxo-
MF   C20 H18 N2 O5
```



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> s l4 full
FULL SEARCH INITIATED 12:22:57 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 10021 TO ITERATE

100.0% PROCESSED 10021 ITERATIONS 61 ANSWERS
SEARCH TIME: 00.00.01

L6 61 SEA SSS FUL L4

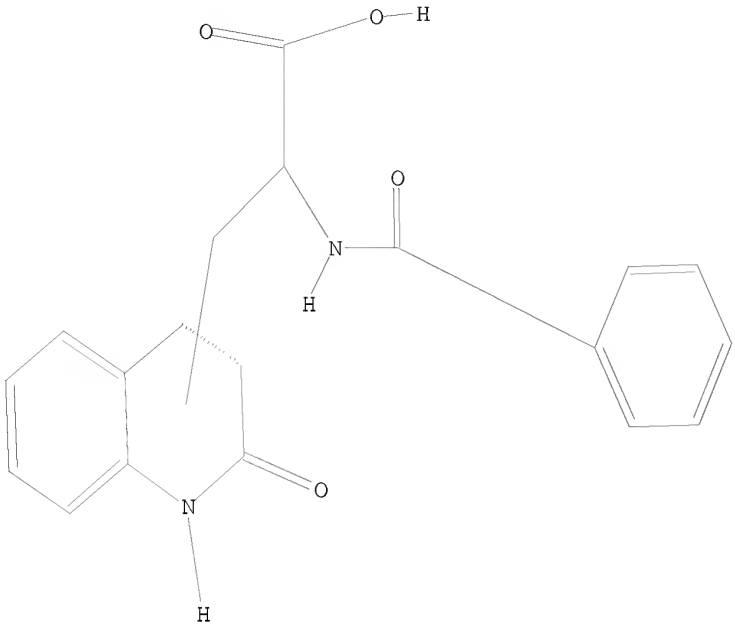
=> file ca

=> s l6
L7 349 L6

=> file reg

L8 STRUCTURE UPLOADED

=> d l8
L8 HAS NO ANSWERS
L8 STR



X

Structure attributes must be viewed using STN Express query preparation.

```
=> s l8 sam
SAMPLE SEARCH INITIATED 12:24:14 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      509 TO ITERATE

100.0% PROCESSED      509 ITERATIONS                                2 ANSWERS
SEARCH TIME: 00.00.01

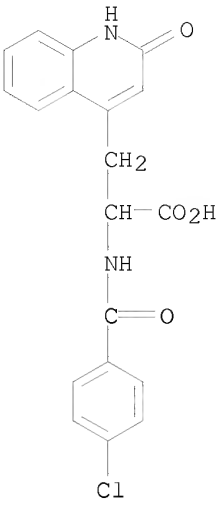
FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         8827 TO    11533
PROJECTED ANSWERS:               2 TO      124

L9            2 SEA SSS SAM L8

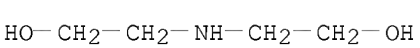
=> d scan

L9   2 ANSWERS   REGISTRY  COPYRIGHT 2009 ACS on STN
IN   4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-
     oxo-, compd. with 2,2'-iminobis[ethanol] (1:1) (9CI)
MF   C19 H15 Cl N2 O4 . C4 H11 N O2

     CM   1
```



CM 2



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> d his

(FILE 'HOME' ENTERED AT 12:21:10 ON 23 JUL 2009)

FILE 'REGISTRY' ENTERED AT 12:21:19 ON 23 JUL 2009
L1 STRUCTURE UPLOADED
L2 0 S L1 SAM
L3 3 S L1 FULL
L4 STRUCTURE UPLOADED
L5 3 S L4 SAM
L6 61 S L4 FULL

FILE 'CA' ENTERED AT 12:23:02 ON 23 JUL 2009
L7 349 S L6

FILE 'REGISTRY' ENTERED AT 12:23:20 ON 23 JUL 2009
L8 STRUCTURE UPLOADED
L9 2 S L8 SAM

=> s l8 subset=l3
ENTER SUBSET SEARCH SCOPE - SAMPLE, FULL, RANGE, OR (END):full
FULL SUBSET SEARCH INITIATED 12:27:36 FILE 'REGISTRY'
FULL SUBSET SCREEN SEARCH COMPLETED - 3 TO ITERATE

100.0% PROCESSED 3 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

L10 0 SEA SUB=L3 SSS FUL L8

=> s l8 full
FULL SEARCH INITIATED 12:27:44 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 10021 TO ITERATE

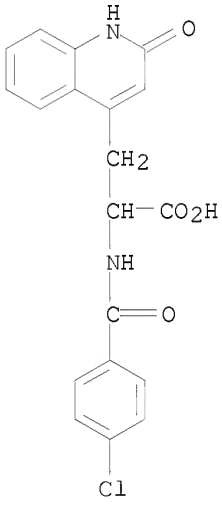
100.0% PROCESSED 10021 ITERATIONS 48 ANSWERS
SEARCH TIME: 00.00.01

L11 48 SEA SSS FUL L8

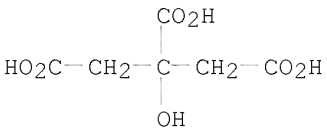
=> d scan

L11 48 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, bismuth(3+) salt, compd. with N,N,N',N'-tetramethylmethanediamine α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo-4-quinolinepropanoate (1:1:1:1)
MF C19 H15 Cl N2 O4 . C6 H8 O7 . C5 H14 N2 . Bi

CM 1

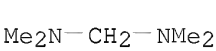


CM 2



● Bi(III)

CM 3



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

```
=> d his

     (FILE 'HOME' ENTERED AT 12:21:10 ON 23 JUL 2009)

     FILE 'REGISTRY' ENTERED AT 12:21:19 ON 23 JUL 2009
L1             STRUCTURE UPLOADED
L2           0 S L1 SAM
L3           3 S L1 FULL
L4             STRUCTURE UPLOADED
L5           3 S L4 SAM
L6          61 S L4 FULL

     FILE 'CA' ENTERED AT 12:23:02 ON 23 JUL 2009
L7         349 S L6

     FILE 'REGISTRY' ENTERED AT 12:23:20 ON 23 JUL 2009
L8             STRUCTURE UPLOADED
L9           2 S L8 SAM
L10          0 S L8  SUB=L3 FULL
L11         48 S L8 FULL

=> file ca


=> s l11
L12        347 L11

=> s l12 and py<
MISSING TERM AFTER PY<
Operators must be followed by a search term, L-number, or query name.

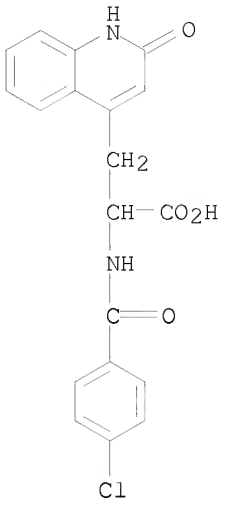
=> s l12 and py<2005
      23749781 PY<2005
L13        234 L12 AND PY<2005
```

```
=> s l13 and carbostyril
          2032 CARBOSTYRIL
L14         14 L13 AND CARBOSTYRIL

=> d ibib abs fhitstr 1-14

L14  ANSWER 1 OF 14  CA  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        131:179816  CA
TITLE:                   Carbostyril derivatives as NADase inhibitors
                         for treatment of gastric ulcer and gastritis
INVENTOR(S):             Noda, Kimitoshi
PATENT ASSIGNEE(S):      Ohtsuka Pharmaceutical Co., Ltd., Japan
SOURCE:                  Jpn. Kokai Tokkyo Koho, 5 pp.
                         CODEN: JKXXAF
DOCUMENT TYPE:           Patent
LANGUAGE:                Japanese
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
     JP 11228413          A     19990824    JP 1998-38607          19980220 <--
PRIORITY APPLN. INFO.:                      JP 1998-38607          19980220
AB   Carbostyril derivs., including
     2-(4-chlorobenzoylamino)-3-(2-quinolon-4-yl)propionic acid, and their
     salts are claimed as NADase inhibitors for treatment of gastric ulcer and
     gastritis.  Formulation examples of tablets, film-coated tablets, and
     injections were given.
IT   90098-04-7
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (carbostyril derivs. as NADase inhibitors for treatment of
        gastric ulcer and gastritis)
RN   90098-04-7  CA
CN   4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-
     oxo-  (CA INDEX NAME)
```

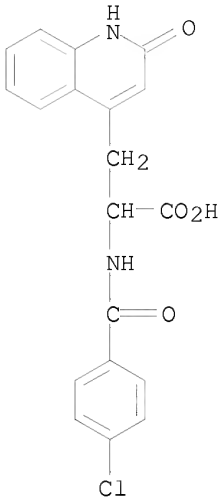


L14 ANSWER 2 OF 14 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 129:86031 CA
ORIGINAL REFERENCE NO.: 129:17653a,17656a
TITLE: ADP-ribosyltransferase inhibitor
INVENTOR(S): Noda, Masatoshi
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan; Noda, Masatoshi
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9826769	A1	19980625	WO 1997-JP4579		19971212	<--
W: AU, BR, CA, CN, ID, KR, MX, SG, US						
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE						
JP 10231246	A	19980902	JP 1997-30139		19970214	<--
JP 10231247	A	19980902	JP 1997-30140		19970214	<--
IN 1997CA02303	A	20050311	IN 1997-CA2303		19971205	
AU 9854109	A	19980715	AU 1998-54109		19971212	<--
PRIORITY APPLN. INFO.:			JP 1996-335462	A	19961216	
			JP 1997-30139	A	19970214	
			JP 1997-30140	A	19970214	
			WO 1997-JP4579	W	19971212	

OTHER SOURCE(S): MARPAT 129:86031
AB The present invention provides a novel ADP-ribosyltransferase inhibitor containing, as the effective ingredient, a carbostyril derivative Tablets were prepared containing 2-(4-chlorobenzoylamino)-3-(2-quinolon-4-yl)propionic acid.
IT 90098-04-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carbostyril derivs. as ADP-ribosyltransferase inhibitors)
RN 90098-04-7 CA
CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



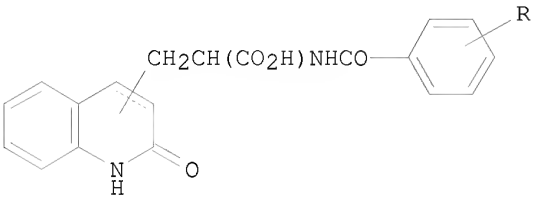
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 14 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 127:9111 CA
ORIGINAL REFERENCE NO.: 127:1833a,1836a
TITLE: Anticancer agents containing carbostyril derivatives
INVENTOR(S): Takahashi, Toshio; Yamane, Tetsuro
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09071532	A	19970318	JP 1995-228889	19950906 <--
CA 2228898	A1	19970313	CA 1996-2228898	19960820 <--
WO 9709045	A1	19970313	WO 1996-JP2319	19960820 <--
W: AU, CA, CN, KR, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9667100	A	19970327	AU 1996-67100	19960820 <--
AU 705751	B2	19990603		
EP 848610	A1	19980624	EP 1996-927200	19960820 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
CN 1195987	A	19981014	CN 1996-196805	19960820 <--

PRIORITY APPLN. INFO.: JP 1995-228889 A 19950906
WO 1996-JP2319 W 19960820

OTHER SOURCE(S): MARPAT 127:9111
GI



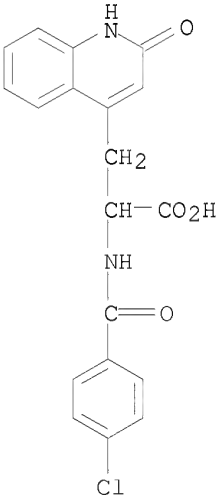
I

AB Anticancer agents, especially useful for digestive tract cancer, contain carbostyril derivs. I (R = halo; the dot line may be double bond) or their salts as active ingredients. Rebamipide at 50 mg/kg/day p.o. for 4 wk remarkably suppressed ENNG-induced duodenal cancer in mice. Some formulation data are also given.

IT 90098-04-7, Rebamipide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticancer agents containing carbostyril derivs. for digestive tract cancer)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



L14 ANSWER 4 OF 14 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 126:334426 CA
ORIGINAL REFERENCE NO.: 126:64925a,64928a
TITLE: Carbostyril derivative for curing ophthalmological diseases
INVENTOR(S): Urashima, Hiroki; Takeji, Yasuhiro; Shinohara, Hisashi; Fujisawa, Shigeki
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan; Urashima, Hiroki; Takeji, Yasuhiro; Shinohara, Hisashi; Fujisawa, Shigeki
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9713515	A1	19970417	WO 1996-JP2850	19961001 <--
W: AU, CA, CN, KR, MX, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
IN 1996CA01696	A	20050304	IN 1996-CA1696	19960925
CA 2234247	A1	19970417	CA 1996-2234247	19961001 <--
CA 2234247	C	20050510		
AU 9670975	A	19970430	AU 1996-70975	19961001 <--
AU 709734	B2	19990902		
EP 859615	A1	19980826	EP 1996-932058	19961001 <--
EP 859615	B1	20010613		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
CN 1202108	A	19981216	CN 1996-198194	19961001 <--
CN 1132580	C	20031231		
ES 2159043	T3	20010916	ES 1996-932058	19961001 <--
TW 446702	B	20010721	TW 1996-85112022	19961002 <--
JP 09301866	A	19971125	JP 1996-269880	19961011 <--
JP 3093661	B2	20001003		
US 6060486	A	20000509	US 1998-51194	19980612 <--
GR 3036457	T3	20011130	GR 2001-401307	20010827 <--
IN 2007KO00323	A	20071005	IN 2007-KO323	20070307

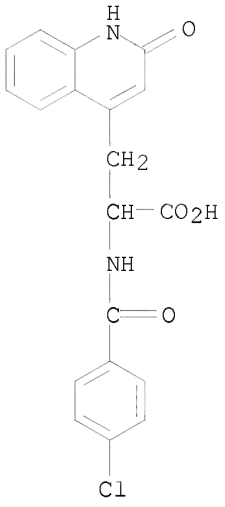
PRIORITY APPLN. INFO.:	JP 1995-263896	A	19951012
	JP 1996-57337	A	19960314
	IN 1996-CA1696	A3	19960925
	WO 1996-JP2850	W	19961001

OTHER SOURCE(S): MARPAT 126:334426

AB The present invention provides an agent for curing ophthalmol. diseases which contains, as the active ingredient, a carbostyril derivative or salt thereof, particularly for curing xerophthalmia (dry eye) syndrome. 2-4-(Chlorobenzoylamino)-3-(2-quinolon-4-yl)propionic acid (I) is preferred compound An eye drop containing I at 0.2 g/100 mL was formulated. Ocular administration of I to rabbits increased the amount of tear fluid, accelerated the proliferation of corneal epithelium, cured mucoid capsulitis, inhibited the injury of the corneal epithelium, and increased the amount of mucoid substance covering on the conjunctiva.

IT 90098-04-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carbostyril derivs. for curing ophthalmol. diseases)

RN 90098-04-7 CA
CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)

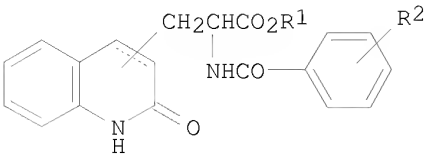


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 14 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 126:74763 CA
ORIGINAL REFERENCE NO.: 126:14472h,14473a
TITLE: Preparation of carbostyril derivative bismuth salts for treatment of ulcer and inflammatory in digestive system
INVENTOR(S): Komatsu, Makoto; Uchida, Minoru; Nishi, Takao; Ishikawa, Hiroshi; Kuroda, Takeshi; Tsuji, Koichi
PATENT ASSIGNEE(S): Otsuka Pharma Co., Ltd., Japan; Ohtsuka Pharmaceutical Co., Ltd.
SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08295673	A	19961112	JP 1995-101908	19950426 <--
JP 3621463	B2	20050216		
PRIORITY APPLN. INFO.:			JP 1995-101908	19950426

OTHER SOURCE(S): MARPAT 126:74763
GI



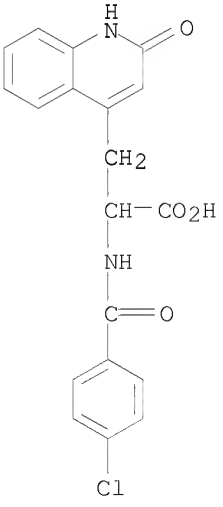
I

AB The title compds. are prepared by reacting carbostyril derivs. (I; R1 = NH2 substituted lower alkyl, R2 = halo, dot line = single or double bond) with carboxylic acid bismuth complex or by reacting I (R1 = H, R2 and dot line = same as above) with carboxylic acid bismuth complex, diamine compds. R3NR4AR5NR6 [II; A = alkylene, p-(A')pC6H4(A'')q; A', A'' = lower alkylene; p, q = 0-1; R3, R4, R5, R6 = (un)substituted alkyl; optionally R3, R4, R5, R6 combine together with N or O to form a 5-6 numbered ring], and piperidine derivs. R7N(CH2CH2)2R8 (III; R7, R8 = H, lower alkyl). The title compds. possessing antibiosis for Helicobacter pylori are useful for treatment of ulcer and inflammatory in digestive system. Thus, 2-hydroxy-1,2,3-propanetricarboxylatobismuth(3+) complex ammonium salt was reacted with Me2NCH2CH2NMe2 and ammonium 2-(4-chlorobenzoylamino)-3-(2-quinolon-4-yl)propionate to give the title compound 2-(4-chlorobenzoylamino)-3-(2-quinolon-4-yl)propionic acid.2-hydroxy-1,2,3-propanetricarboxylatobismuth(3+).Me2NCH2CH2NMe2 salt (IV). IV at 449 mg/kg p.o. inhibited the proliferation of H. pylori in mouse stomach. A tablet containing IV was also prepared

IT 90098-04-7DP, bismuth complex
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of carbostyril derivative bismuth salts for treatment of ulcer and inflammatory in digestive system)

RN 90098-04-7 CA

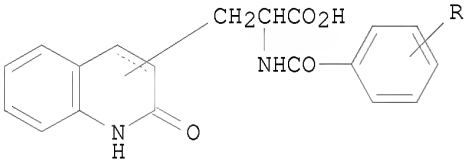
CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



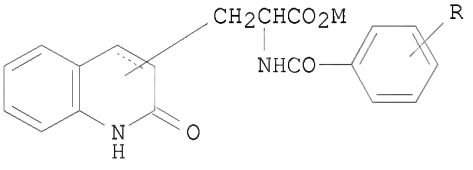
L14 ANSWER 6 OF 14 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 123:313783 CA
ORIGINAL REFERENCE NO.: 123:56247a,56250a
TITLE: Preparation of bismuth salts of carbostyril derivatives for the treatment of Helicobacter pylori-induced peptic ulcers
INVENTOR(S): Komatsu, Makoto; Uchida, Minoru; Nishi, Takao
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9512579	A1	19950511	WO 1994-JP1805	19941027 <--
W: AU, CA, CN, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9480031	A	19950523	AU 1994-80031	19941027 <--
PRIORITY APPLN. INFO.:			JP 1993-276745 A	19931105
			WO 1994-JP1805 W	19941027

OTHER SOURCE(S): CASREACT 123:313783; MARPAT 123:313783
GI



I



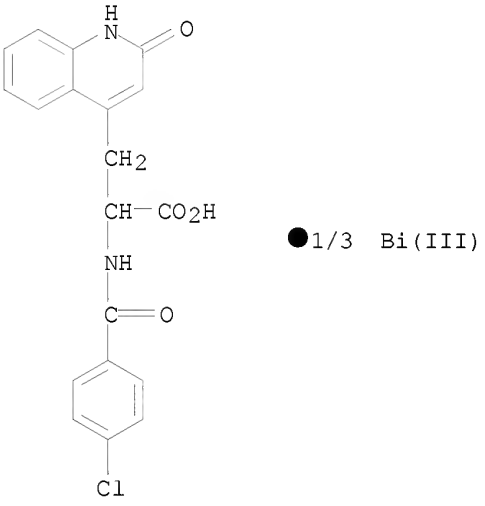
II

AB The title Bi salt compds. (I; R = halogen; the propionic acid substituent is substituted at the 3- or 4-position on the carbostyril nucleus and the bond between the 3- and 4-positions is a single or double bond), useful for the prevention and treatment of Helicobacter pylori-induced peptic ulcers and peptic inflammatory diseases, are prepared by the reaction of propionate salts (II; M = alkali metal) with bismuth nitrate (III), and I-containing formulations are presented. Thus, 2-(4-chlorobenzoylamino)-3-(2-quinolon-4-yl)propionic acid was neutralized with NaOH and the corresponding Na salt reacted with III, producing Bi

2-(4-chlorobenzoylamino)-3-(2-quinolon-4-yl)propionate [IV; m.p. 248-257° (decomposition)]. IV demonstrated a MIC against Helicobacter pylori (ATCC 43504) of 3.98 μg/g.

IT 169809-60-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bismuth salts of carbostyril derivs. for the treatment of Helicobacter pylori-induced peptic ulcers)

RN 169809-60-3 CA
CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo-, bismuth(3+) salt (3:1) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 14 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 123:47906 CA
ORIGINAL REFERENCE NO.: 123:8383a,8386a
TITLE: Carbostyril derivative for inhibiting production of interleukin-8
INVENTOR(S): Matsuda, Takahide; Owada, Shigeru; Muta, Hiroshi; Aihara, Miki; Takizawa, Hisao; Imagawa, Ken-ichi; Kikuchi, Mikio
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9511026	A1	19950427	WO 1994-JP1739	19941017 <--

W: AU, CA, CN, KR, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

CA 2150546	A1	19950427	CA 1994-2150546	19941017 <--
CA 2150546	C	20041109		
AU 9478641	A	19950508	AU 1994-78641	19941017 <--
AU 683697	B2	19971120		
EP 674515	A1	19951004	EP 1994-929670	19941017 <--
EP 674515	B1	19990922		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

JP 08012578	A	19960116	JP 1994-250473	19941017 <--
JP 2839847	B2	19981216		
CN 1117268	A	19960221	CN 1994-190812	19941017 <--
CN 1073418	C	20011024		
AT 184793	T	19991015	AT 1994-929670	19941017 <--
ES 2138092	T3	20000101	ES 1994-929670	19941017 <--
US 5637597	A	19970610	US 1995-448577	19950607 <--
GR 3032091	T3	20000331	GR 1999-403182	19991208 <--

PRIORITY APPLN. INFO.:	JP 1993-263417 A	19931021
	JP 1993-263418 A	19931021
	JP 1993-263419 A	19931021
	JP 1994-89641 A	19940427
	WO 1994-JP1739 W	19941017

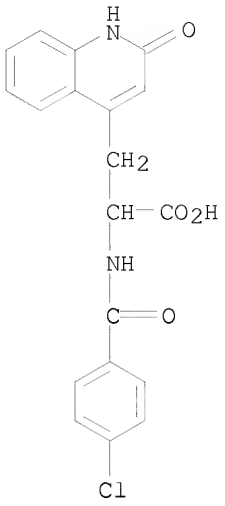
OTHER SOURCE(S): MARPAT 123:47906

AB Carbostyril derivs. are useful for inhibiting production of interleukin-8, inhibiting granulocyte activation, and curing inflammatory diseases. Thus, 2-(4-chlorobenzoylamino)-3-(2-quinolon-4-yl)propionic acid (I) (100 mg orally 3 times a day for 6 mo) decreased the number and severity of oral aphthous ulcers in patients with Behcet's disease. Tablets were prepared from a mixture of I 150, citric acid 1.0, lactose 33.5, di-Ca phosphate 70.0, Pluronic F-68 30.0, SDS 18.0, PVP 15.0, Carbowax 1500 4.5, Carbowax 6000 45.0, corn starch 30.0, and Mg stearate 3.0 g.

IT 90098-04-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carbostyril derivative for inhibiting production of interleukin-8)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 14 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 121:117721 CA
ORIGINAL REFERENCE NO.: 121:21085a,21088a
TITLE: Carbostyril derivatives for preventing and treating disturbances of intestinal mucous membrane
INVENTOR(S): Yamasaki, Katsuya; Sakurai, Kazushi; Akiyama, Kazue; Osaka, Toshihiro
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co. Ltd., Japan
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9412182	A1	19940609	WO 1993-JP1700	19931119 <--
W: AU, CA, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 06211662	A	19940802	JP 1993-231353	19930917 <--
JP 2872546	B2	19990317		
CA 2128094	A1	19940609	CA 1993-2128094	19931119 <--
AU 9455340	A	19940622	AU 1994-55340	19931119 <--
AU 668267	B2	19960426		
EP 621782	A1	19941102	EP 1994-900289	19931119 <--
R: CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
CN 1095593	A	19941130	CN 1993-114962	19931126 <--
CN 1040176	C	19981014		
US 5576331	A	19961119	US 1994-256372	19940722 <--

PRIORITY APPLN. INFO.: JP 1992-316852 A 19921126
JP 1993-231353 A 19930917

WO 1993-JP1700 W 19931119

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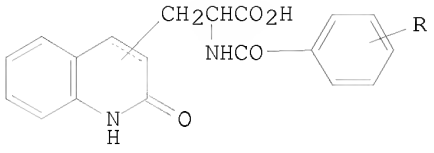


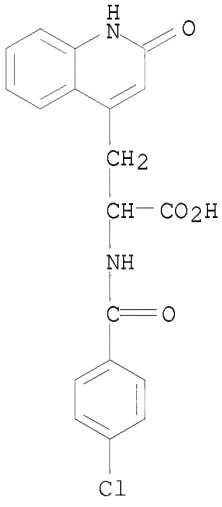
I

AB An agent for preventing and treating disturbance of intestinal mucous membrane comprises, as the active ingredient, a carbostyril derivative I (R = halogen) or a salt thereof. A tablet formulation contained 2-(4-chlorobenzoylamino)-3-(2-quinolon-4-yl)propionic acid 150.0, citric acid 1.0, lactose 33.5, CaHPO4 70.0, Pluronic F68 30.0, SLS 15.0, PVP 15.0, Carbowax 1500 4.5, Carbowax 6000 45.0, starch 30.0, Mg stearate 3.0, and dried SLS 3.0 g, resp. Tablets were prepared by a wet granulation method; anti-inflammatory effects of tablets obtained against acetic acid-induced ulcerative colitis were demonstrated in rats.

IT 90098-04-7
RL: BIOL (Biological study)
(tablets containing, anti-inflammatory activity of, in intestine)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 14 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 120:116844 CA
ORIGINAL REFERENCE NO.: 120:20447a,20450a
TITLE: Pharmaceutical compositions containing

carbostyril derivatives for increasing or inhibiting decrease of somatostatin

INVENTOR(S): Yamasaki, Katsuya; Sakurai, Kazushi
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan

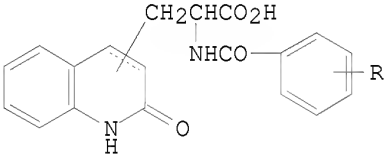
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9323043	A1	19931125	WO 1993-JP545	19930427 <--
W: AU, CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9340229	A	19931213	AU 1993-40229	19930427 <--
AU 657412	B2	19950309		
EP 594867	A1	19940504	EP 1993-909427	19930427 <--
R: CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
JP 06509587	T	19941027	JP 1993-520044	19930427 <--
JP 2702284	B2	19980121		
CN 1080851	A	19940119	CN 1993-106046	19930514 <--
CN 1038903	C	19980701		
US 5476858	A	19951219	US 1994-193124	19940105 <--

PRIORITY APPLN. INFO.: JP 1992-121791 A 19920514
WO 1993-JP545 A 19930427

OTHER SOURCE(S): MARPAT 120:116844

GI



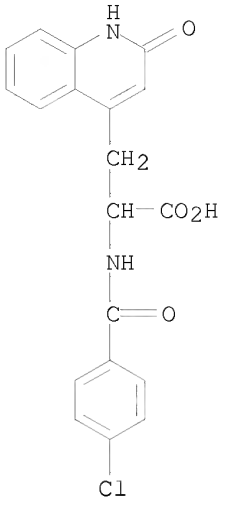
II

AB Pharmaceutical compns. for treatment of diseases associated with the decrease of somatostatin (I), e.g. esophagitis, comprise an carbostyril derivative (II; R=halogen). Rats were given 5mM Na taurocholate (III) with drinking water for 6 mo after which the administration of III was stopped and 2-(4-chlorobenzoylamino)-3-(2-quinolon-4-yl)propionic acid (IV) in doses of 60 mg/kg/day was administered for 4 wks, then rats were killed and the stomach was removed. The amount of I in stomach mucosal membrane for the animals who were administered IV was 40.7 as compared to 45.4 for controls, and 19.1 for those who received III. A tablet containing 150g I was prepared

IT 90098-04-7
RL: BIOL (Biological study)
(pharmaceutical composition containing, as somatostatin stimulants)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



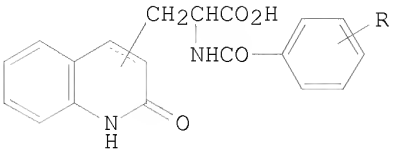
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 10 OF 14 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 118:109733 CA
ORIGINAL REFERENCE NO.: 118:19025a,19028a
TITLE: Carbostyril derivatives as antidiabetics
INVENTOR(S): Yamasaki, Katsuya; Sakurai, Kazushi; Akiyama, Kazue
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9221342	A1	19921210	WO 1992-JP689	19920528 <--
W: AU, CA, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
CA 2088582	A1	19921208	CA 1992-2088582	19920528 <--
AU 9217833	A	19930108	AU 1992-17833	19920528 <--
AU 645690	B2	19940120		
EP 543018	A1	19930526	EP 1992-911055	19920528 <--
EP 543018	B1	19960110		
R: CH, DE, DK, FR, GB, IT, LI, NL, SE				
JP 05148143	A	19930615	JP 1992-138510	19920529 <--
US 5480891	A	19960102	US 1993-159703	19931201 <--

PRIORITY APPLN. INFO.:
JP 1991-136465 A 19910607
WO 1992-JP689 A 19920528
US 1993-978696 B1 19930205

OTHER SOURCE(S): MARPAT 118:109733
GI



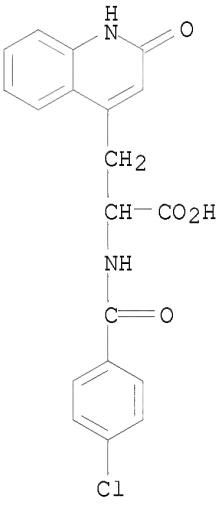
I

AB The antidiabetics are I (R = halo; the side chain is on 3 or 4 position) which are effective in decreasing blood sugar and controlling blood insulin level. Tablets were prepared containing 2-(4-chlorobenzoylamino)-3-(2-quinolon-4-yl)propionic acid.

IT 90098-04-7
RL: BIOL (Biological study)
(as antidiabetic)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 11 OF 14 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 116:51580 CA

ORIGINAL REFERENCE NO.: 116:8751a,8754a

TITLE: Pharmaceuticals containing carbostyrils or their salts for treatment of gastritis

INVENTOR(S): Yamazaki, Katsuya; Yabuchi, Yoichi

PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF

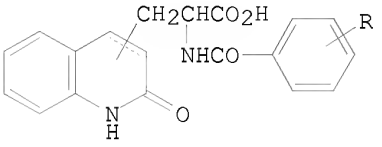
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 03074329	A	19910328	JP 1989-210504	19890814 <--
JP 2812998	B2	19981022		
PRIORITY APPLN. INFO.:			JP 1989-210504	19890814
OTHER SOURCE(S):	MARPAT 116:51580			

GI



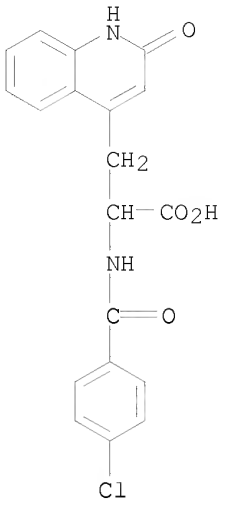
I

AB The title pharmaceuticals contain carbostyrils I (R = halo; the substituted position in the carbostyril skeleton is 3- or 4-position; the bonding between 3- and 4-positions in the carbostyril skeleton is single or double bond) or their salts as active ingredients. Tablets were prepared from 2-(4-chlorobenzoylamino)-3-(2-quinolone-4-yl)propionic acid (II) 150, Avicel 40, corn starch 30, and Mg stearate 2 g, which was coated with a mixture of (hydroxypropyl)methylcellulose 10, polyethylene glycol 6000 3, castor oil 40, and MeOH 40 g to give film-coating tablets. II at 100 mg/kg p.o. showed 77% repression rate against gastric mucosal injury caused by HCl-taurocholic acid in rats.

IT 90098-04-7
RL: BIOL (Biological study)
(pharmaceuticals containing, for treatment of gastritis)

RN 90098-04-7 CA

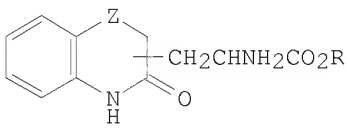
CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



L14 ANSWER 12 OF 14 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 115:279834 CA
ORIGINAL REFERENCE NO.: 115:47551a,47554a
TITLE: Preparation of carbostyril derivatives as intermediates for gastric ulcer inhibitors
INVENTOR(S): Otsubo, Kenji; Morita, Seiji; Uchida, Minoru; Shimizu, Takefumi
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 03145468	A	19910620	JP 1989-281397	19891028 <--
JP 2820739	B2	19981105		
PRIORITY APPLN. INFO.:			JP 1989-281397	19891028
OTHER SOURCE(S):	MARPAT 115:279834			

GI



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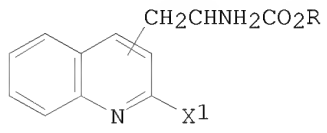


III

AB Optically active title derivs. I (R = H, Z = CH:CH) (II) and their salts are prepared by hydrolysis of optically active haloquinolines III (R = lower

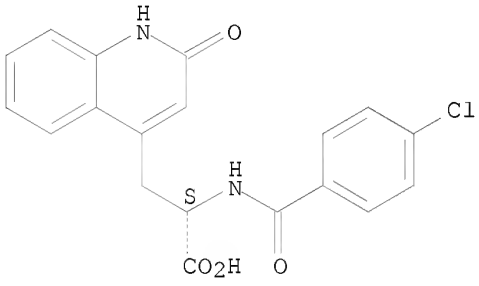
alkyl; X1 = halo). Optically active I (Z = CH2CH2, CH:CH; R = lower alkyl) and their salts are prepared by optical resolution Refluxing 300 mg (S)-(-)-Me 2-amino-3-(2-chloroquinolin-4-yl)propionate [prepared from (3R)-2,5-dimethoxy-3-isopropyl-3,6-dihydropyrazine and 4-(bromomethyl)-2-chloroquinoline] in aqueous HCl for 6 h gave 168 mg (S)-II.HCl in 98.4% e.e., 148 mg of which was treated with 106 mg p-ClC6H4COCl in Me2CO-H2O at 0° for 2 h to give 112.5 mg (S)-(-)-2-(4-chlorobenzoylamino)-3-(2-quinolon-4-yl)propionic acid (≥99.5% e.e.).

IT 111911-88-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as ulcer inhibitor)

RN 111911-88-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 13 OF 14 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 106:50063 CA

ORIGINAL REFERENCE NO.: 106:8291a,8294a

TITLE: Carbostyril derivatives

PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 78 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

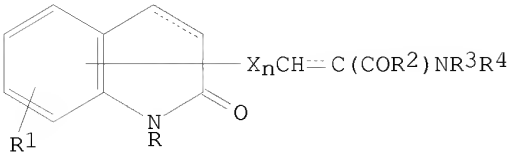
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
JP 60019767	A	19850131	JP 1983-126498	19830711	<--
JP 02061923	B	19901221			
JP 01308258	A	19891212	JP 1989-109540	19890427	<--
JP 05009429	B	19930204			
JP 05065273	A	19930319	JP 1992-55120	19920313	<--

PRIORITY APPLN. INFO.: JP 1983-126498 19830711
JP 1989-109540 19890427

OTHER SOURCE(S): CASREACT 106:50063

GI



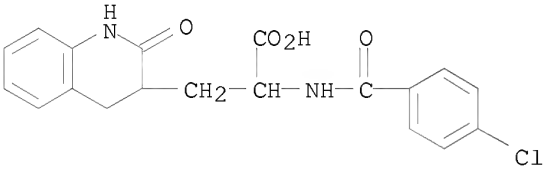
I

AB The title compds. [I; R = H, alkyl, alkenyl, alkynyl, phenylalkyl; R1 = H, halo, OH, (substituted) BzO, alkyl, alkoxy; R2 = OH, NH2, cycloalkylalkylamino, alkoxy, alkoxycarbonylalkoxy, etc.; R3 = H, OH, substituted PhSO2, etc.; R4 = H, substituted PhSO2; X = alkylene; n = 0, 1], useful as antiulcer agents, are prepared Thus, refluxing a mixture of 5 g Et 2-acetamido-2-carboxy-3 (1,2-dihydro-2-oxo-4-quinolinyl)propionate [obtained by treating 4-(bromomethyl)carbostyril with AcNHCH(CO2Et) in HOEt/NaOEt] and 150 mL 20% HCl for 9 h gave 3.2 g 2-amino-3-(1,2-dihydro-2-oxo-4-quinolinyl)propionic acid-HCl.H2O. At 10 mg/kg orally twice daily 37 tested I inhibited ulcers by 13.5-38.5% in rats.

IT 90098-00-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as anti-ulcer agent)

RN 90098-00-3 CA

CN 3-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2,3,4-tetrahydro-2-oxo- (CA INDEX NAME)



L14 ANSWER 14 OF 14 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 101:54936 CA

ORIGINAL REFERENCE NO.: 101:8532h,8533a

TITLE: Carbostyril derivatives and pharmaceuticals containing them

INVENTOR(S): Uchida, Minoru; Komastu, Makoto; Nakagawa, Kazuyuki

PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan

SOURCE: Ger. Offen., 198 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

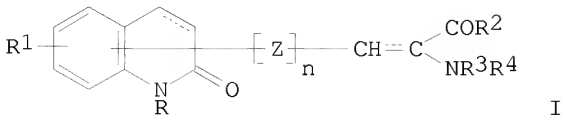
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3324034	A1	19840105	DE 1983-3324034	19830704 <--
DE 3324034	C2	19930701		
JP 59007168	A	19840114	JP 1982-117311	19820705 <--
JP 63035623	B	19880715		

JP 59007169	A	19840114	JP 1982-117312	19820705	<--
JP 03028425	B	19910419			
FI 8302425	A	19840106	FI 1983-2425	19830701	<--
FI 80022	B	19891229			
FI 80022	C	19900410			
US 4578381	A	19860325	US 1983-510241	19830701	<--
BE 897208	A1	19840104	BE 1983-211114	19830704	<--
DK 8303078	A	19840106	DK 1983-3078	19830704	<--
DK 168288	B1	19940307			
NO 8302431	A	19840106	NO 1983-2431	19830704	<--
NO 164835	B	19900813			
NO 164835	C	19901121			
SE 8303813	A	19840106	SE 1983-3813	19830704	<--
SE 462848	B	19900910			
SE 462848	C	19910117			
AU 8316536	A	19840112	AU 1983-16536	19830704	<--
AU 552717	B2	19860619			
CH 654578	A5	19860228	CH 1983-3667	19830704	<--
AT 8302451	A	19870915	AT 1983-2451	19830704	<--
AT 385506	B	19880411			
CA 1247624	A1	19881227	CA 1983-431763	19830704	<--
FR 2530626	A1	19840127	FR 1983-11179	19830705	<--
FR 2530626	B1	19861205			
NL 8302390	A	19840201	NL 1983-2390	19830705	<--
NL 194165	B	20010402			
NL 194165	C	20010803			
GB 2123825	A	19840208	GB 1983-18174	19830705	<--
GB 2123825	B	19850918			
ZA 8304901	A	19840328	ZA 1983-4901	19830705	<--
ES 530715	A5	19850614	ES 1984-530715	19840316	<--
JP 63190879	A	19880808	JP 1987-314429	19871211	<--
JP 02042828	B	19900926			
US 34722	E	19940906	US 1992-937382	19920831	<--

PRIORITY APPLN. INFO.:

JP 1982-117311	A	19820705
JP 1982-117312	A	19820705
US 1983-510241	A5	19830701

OTHER SOURCE(S): MARPAT 101:54936
GI



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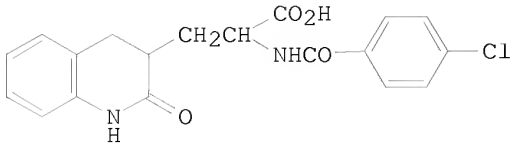
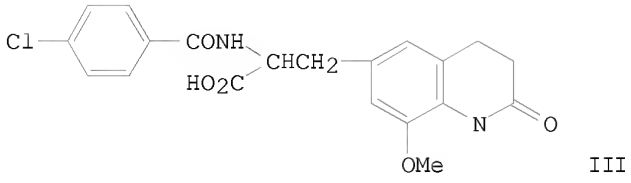


II



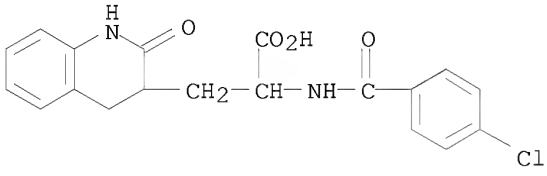
III

AB Title compds. I [R = H, lower alkyl, alkenyl, alkynyl, phenylalkyl; R1 = H, halo, (halo)benzoyloxy, OH, lower alkyl, alkoxy; R2 = OH, acid derivative; R3 = H, aroyl, arylsulfonyl, etc.; R4 = H, arylsulfonyl; Z = lower alkylene, n = 0, 1; dotted lines signify possible double bonds] and intermediates for them (.apprx.220 in all) were prepared in several conventional ways and shown in some cases to be more active as ulcer-healing agents than sucralfat. Typical of compds. prepared and tested were II and III.

IT 90098-00-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antiulcer activity of)

RN 90098-00-3 CA

CN 3-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2,3,4-tetrahydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L2             0 S L1 SAM
L3             3 S L1 FULL
L4               STRUCTURE UPLOADED
L5             3 S L4 SAM
L6            61 S L4 FULL

     FILE 'CA' ENTERED AT 12:23:02 ON 23 JUL 2009
L7           349 S L6

     FILE 'REGISTRY' ENTERED AT 12:23:20 ON 23 JUL 2009
L8               STRUCTURE UPLOADED
L9             2 S L8 SAM
L10            0 S L8  SUB=L3 FULL
L11           48 S L8 FULL

     FILE 'CA' ENTERED AT 12:27:59 ON 23 JUL 2009
L12          347 S L11
L13          234 S L12 AND PY<2005
L14           14 S L13 AND CARBOSTYRIL

=> s l13 not l14
L15         220 L13 NOT L14

=> d 1-50 ibib abs fhitstr

L15  ANSWER 1 OF 220  CA  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        145:271648  CA
TITLE:                   Rebamipide lysinate and rebamipide argininate and
                         pharmaceutical preparation containing the same as
                         active substance
INVENTOR(S):             Kim, Uk; Noh, Jae Il
PATENT ASSIGNEE(S):      Jin Yang Pharm. Co., Ltd., S. Korea
SOURCE:                  Repub. Korean Kongkae Taeho Kongbo, No pp. given
                         CODEN: KRXXA7
DOCUMENT TYPE:           Patent
LANGUAGE:                Korean
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
     KR 2004104020        A     20041210    KR 2003-35382          20030602 <--
PRIORITY APPLN. INFO.:                      KR 2003-35382          20030602
AB   Rebamipide lysinate and rebamipide argininate and a pharmaceutical preparation
     containing the same as active substance, which rebamipide lysinate and
     rebamipide argininate have improved solubility in solvent and reactivity, so
     that it can be useful for treatment of gastric ulcer, acute gastritis and
     chronic gastritis, are provided.  The rebamipide lysinate and rebamipide
     argininate are prepared by reacting rebamipide with L-lysine and L-arginine
     in an equivalent ratio of 1:1 to 1:5.  The pharmaceutical preparation contains
the
     rebamipide lysinate and rebamipide argininate as the active substance.
IT   847165-02-0P, Rebamipide lysinate
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL
     (Biological study); PREP (Preparation)
```

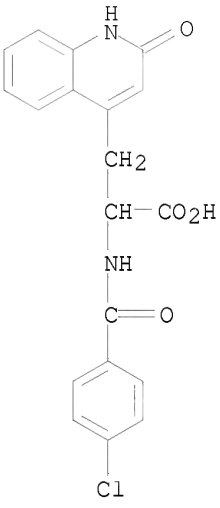
(rebamipide lysinate and rebamipide argininate and pharmaceutical preparation containing the same as active substance)

RN 847165-02-0 CA

CN L-Lysine, mono[α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo-4-quinolinepropanoate] (9CI) (CA INDEX NAME)

CM 1

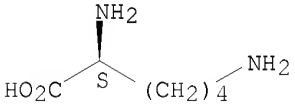
CRN 90098-04-7
CMF C19 H15 Cl N2 O4



CM 2

CRN 56-87-1
CMF C6 H14 N2 O2

Absolute stereochemistry.



L15 ANSWER 2 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 143:126379 CA

TITLE: Induction of cyclooxygenase-2 in rat gastric mucosa by rebamipide

AUTHOR(S): Sun, Weihao; Yu, Qian; Ou, Xilong; Cao, Dazhong; Yu, Ting; Zhu, Feng; Fu, Xiling

CORPORATE SOURCE: Department of Gastroenterology, Affiliated Zhongda Hospital of Southeast University, Nanjing, 210009, Peop. Rep. China

SOURCE: Zhongguo Yaolixue Tongbao (2003), 19(12),

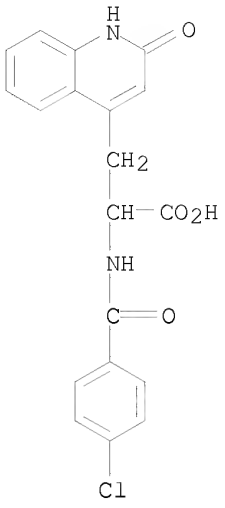
1393-1396
CODEN: ZYTOE8; ISSN: 1001-1978
PUBLISHER: Anhui Yike Daxue Linchuan Yaoli Yanjiuso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Recent studies indicate an expression of mitogen-inducible cyclooxygenase(COX-2) in gastric mucosa. Rebamipide, a mucoprotective agent, has been reported to prevent various acute exptl. gastric mucosal lesions and to accelerate the healing of chronic ulcers. However, the precise mechanisms of gastroprotection are unclear. The relationship between protective effects of rebamipide and COX-2 expression was studied in rat gastric mucosa. Male Sprague dawley rate were given 5, 15 and 50 mg/kg d of rebamipide for two weeks. The expression of COX-1 and COX-2 in gastric mucosa was determined by western blot anal. and immunohistochem. staining. The level of PGE2 in gastric mucosa was measured by enzyme immune assay. The protective action of rebamipide against gastric injury caused by 0.6 mol/L HCl was investigated. Effects of a specific COX-2 inhibitor NS-398 on the PGE2 synthesis in gastric mucosa and the mucosal protection afforded by rebamipide were evaluated. COX-2 expression was enhanced, while COX-1 expression did not change significantly in stomach after treatment with rebamipide. The gastric mucosal PGE2 levels were (2293±373), and (3933±667) pg/g wet wt in the groups treated with 5, 15, or 50 mg/kg of rebamipide resp., which were significantly higher than that in the control group (1467±400) pg/g wet wt($P < 0.05$). The lesion index induced by HCl were (2.11±0.61)%, %, (1.04±0.23)% resp. in the rebamipide groups and (3.63±0.96)% in the control group($P < 0.05$). A specific COX-2 inhibitor blocked the rebamipide induced increase in mucosal PGE2, and mucosal protection induced by rebamipide. This study demonstrates that rebamipide induces COX-2 expression, increases PGE, level, and enhances gastric mucosal defense in a COX-2 dependent manner. Thus, COX-2 plays an important role in the effects of rebamipide on gastric mucosal protection.

IT 90098-04-7, Rebamipide
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(induction of cyclooxygenase-2 in rat gastric mucosa by rebamipide)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



L15 ANSWER 3 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 143:19670 CA
TITLE: Protective Effect of Intra-Rectal Administration of Rebamipide on Dextran Sulfate Sodium-Induced Rat Colitis
AUTHOR(S): Okayama, Mitsuaki; Tsubouchi, Ryoichi; Nishio, Hikaru; Kato, Shinichi; Takeuchi, Koji
CORPORATE SOURCE: Department of Pharmacology and Experimental Therapeutics, Kyoto Pharmaceutical University, Kyoto, Japan
SOURCE: Digestion (2004), 70(4), 240-249
CODEN: DIGEBW; ISSN: 0012-2823
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

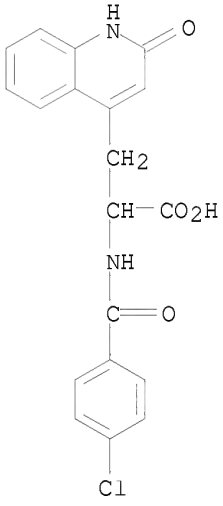
AB Background/Aim: Rebamipide, an anti-ulcer drug, has various actions including radical scavenging and mucus-stimulating as well as anti-inflammatory effects, and exhibits both mucosal protective and healing promoting actions in the stomach. In the present study, we examined the effect of rebamipide on an animal model of colitis induced by dextran sulfate sodium (DSS). Methods: Exptl. colitis was induced in rats by daily treatment with 3% DSS in drinking water for 7 days. Rebamipide (3-30 mg/kg), 5-aminosalicylic acid (5-ASA: 150 mg/kg) or metronidazole (10 and 30 mg/kg) was administered intra-rectally once daily for 6 days. The ulceration area, colon length, and mucosal myeloperoxidase (MPO) activity as well as thiobarbituric acid-reactive substance (TBARS) were measured on the 7th day after the onset of DSS treatment. The effects of rebamipide on the secretion of mucus in the colon was also examined Results: DSS treatment caused severe lesions in the colon, accompanied by an increase in MPO activity and TBARS as well as a decrease in body weight gain and colon length. Repeated administration of rebamipide dose-dependently suppressed the colon lesions and improved the pathol. changes induced by DSS treatment. Rebamipide significantly increased the mucus contents in the colon. Both 5-ASA and metronidazole also reduced

the severity of DSS-induced lesions. Conclusion: These results suggest that intra-rectal administration of rebamipide is effective against DSS-induced colitis. The protective effect of rebamipide may be attributable to both the radical scavenging action and the increase in the production of mucus in the colon, the latter presumably suppressing the process of intestinal bacterial infiltration.

IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(intra-rectal administration of rebamipide dose-dependently suppressed colon lesions and improved MPO activity and TBARS, pathol. changes and significantly increased mucus contents in colon on rat model of colitis induced by DSS)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 142:441625 CA

TITLE: Effector sites of gastroprotective agents by in vitro autoradiography: comparison of rebamipide, teprenone and sofalcone

AUTHOR(S): Nakamura, Masahiko; Tsuchimoto, Kanji

CORPORATE SOURCE: Center for Clinical Pharmacy and Clinical Sciences, School of Pharmaceutical Sciences, Kitasato University, Japan

SOURCE: Japanese Pharmacology & Therapeutics (2004), 32(12), 909-913
CODEN: JPTABU

PUBLISHER: Raifu Saiensu Shuppan K.K.

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

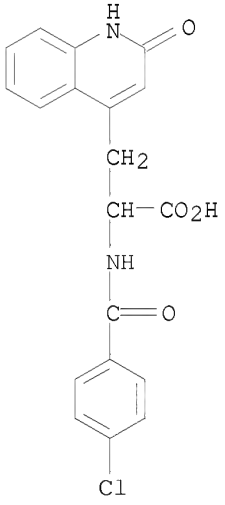
AB Objectives One of the major clin. effects of gastroprotective drugs, used

in patients with gastric ulcers, is alleviation of symptoms. These drugs are reported to act on various sites in the stomach. Now, relatively active arguments have been made within the framework of reevaluation of this kind of drugs from the standpoint of evidence-based medicine. The present study was undertaken to examine uptake sites of rebamipide, teprenone and sofalcone, in an effort to re-evaluate gastroprotective drugs. Methods Unfixed gastric fundic specimens from male Wistar rats were used for in vitro autoradiog. in combination with indirect immunohistochem. staining. The distributions of the three drugs (rebamipide, teprenone and sofalcone) in specimens were analyzed, to explore differences in the pharmacol. actions of these drugs in comparison with the actions reported in the literature. Results In the present study, rebamipide, teprenone and sofalcone were all found to bind to surface mucous cells, suggesting that these drugs are involved in potentiation of the gastric mucosal defense system. In specimens of gastric mucosa affected by acetic acid-induced ulcers, rebamipide was found to bind to inflammatory cells, while teprenone bound to the lamina propria at the ulcer base and sofalcone to submucosal tissue in the vicinity of the microcirculatory system. Conclusion The differences of the binding sites among these three drugs appear to be associated with the differences in their pharmacol. activity. Notably, the binding of rebamipide to inflammatory cells may be closely related to the anti-ulcer activity of this drug.

IT 90098-04-7, Rebamipide
RL: DMA (Drug mechanism of action); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effector sites of gastroprotective agents by in vitro autoradiog., comparison of rebamipide, teprenone and sofalcone)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



L15 ANSWER 5 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 142:284931 CA

TITLE: Oral Absorption and Pharmacokinetics of Rebamipide and

Rebamipide Lysinate in Rats

AUTHOR(S): Shin, Beom Soo; Kim, Chul Hwan; Jun, Yoon Sik; Yoon, Chi Ho; Rho, Jae Il; Lee, Kang Choon; Han, Hye Seon; Yoo, Sun Dong

CORPORATE SOURCE: College of Pharmacy, Sungkyunkwan University, Kyeonggi-do, S. Korea

SOURCE: Drug Development and Industrial Pharmacy (2004), 30(8), 869-876
CODEN: DDIPD8; ISSN: 0363-9045

PUBLISHER: Marcel Dekker, Inc.

DOCUMENT TYPE: Journal

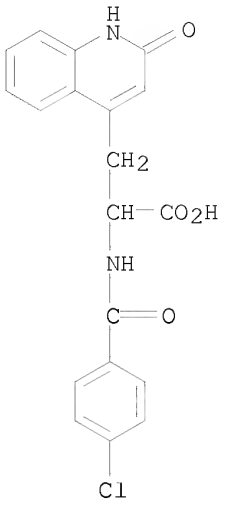
LANGUAGE: English

AB Rebamipide is an anti-ulcer agent exhibiting a low aqueous solubility and a poor oral bioavailability. This study was conducted to examine if the rebamipide lysinate salt form would exhibit improved solubility profiles and higher oral bioavailability compared with rebamipide free acid. Both compds. showed pH-dependent solubility profiles, with the solubility of rebamipide lysinate dramatically improved at a median pH of 5.1 (17-fold increases) over free acid, but the improvement in the solubility was not as pronounced in artificial gastric and intestinal fluids (1.4- and 1.9-fold increases, resp.). The Cl, Vss and t1/2 in rats after i.v. injection of rebamipide (0.5 mg/kg) averaged 21.0±3.2 mL/min/kg, 0.3±0.0 L/kg, and 0.4±0.1 h, resp. No significant difference was observed in these parameters between rebamipide and rebamipide lysinate. Despite improved solubility profiles, the absolute oral bioavailability of rebamipide lysinate was not increased (5.1 vs. 4.8%) nor did AUC (407.8 vs. 383.6 ng.hr/mL) and Cmax (87.4 vs.77.0 ng/mL) compared with rebamipide free acid. Rebamipide lysinate, however, showed a more rapid absorption, and initial serum drug concns. were higher than those found for rebamipide free acid.

IT 90098-04-7, Rebamipide
RL: PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral absorption and pharmacokinetics of rebamipide and rebamipide lysinate in rats)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 142:176706 CA
TITLE: Process for preparing rebamipide
INVENTOR(S): Hong, Hyeon Su; Jung, Yong Ho; Kang, So Yeon; Kwon, O. Jin; Lim, Jae Gyeong; Oh, Yun Seok
PATENT ASSIGNEE(S): Dong Wha Pharm. Ind. Co., Ltd., S. Korea
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2003050412	A	20030625	KR 2001-80842	20011218 <--
KR 766578	B1	20071011		

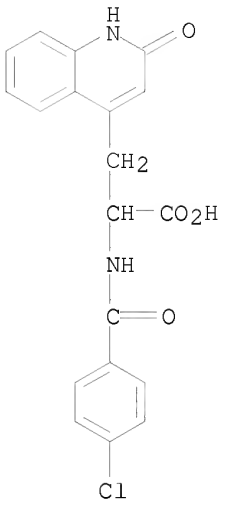
PRIORITY APPLN. INFO.: KR 2001-80842 20011218

AB A process for preparing rebamipide is provided, thereby simplifying the preparing process of rebamipide and improving the preparation yield of rebamipide.

A process for preparing rebamipide of the formula(1) comprises the steps of: reacting 4-(bromomethyl)-1,2-dihydro-2-quinolinone of formula(2) with di-Et 2-[(4-chlorobenzoyl)amino]malonate of formula(3) to prepare a compound of formula(4); and reacting the compound of formula(4) under basic conditions, wherein R is alkyl having the carbon number of 1 to 6, wherein the di-Et 2-[(4-chlorobenzoyl)amino]malonate of formula(3) is prepared by reacting di-Et 2-aminomalonate hydrochloride with 4-chlorobenzoyl derivative of formula(6); and R is alkyl having the carbon number of 1 to 6 and X is OH or halogen atom.

IT 90098-04-7P, Rebamipide
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of rebamipide)
RN 90098-04-7 CA
CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



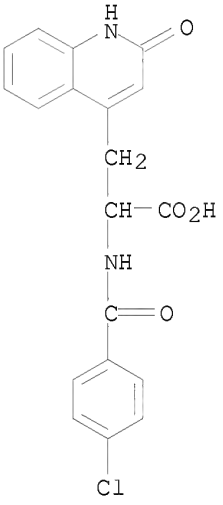
L15 ANSWER 7 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 142:62453 CA
TITLE: Development of suppository formulation safely improving rectal absorption of rebamipide, a poorly absorbable drug, by utilizing sodium laurate and taurine
AUTHOR(S): Miyake, Masateru; Kamada, Naoki; Oka, Yoshikazu; Mukai, Tadashi; Minami, Takanori; Toguchi, Hajime; Odomi, Masaaki; Ogawara, Kenichi; Higaki, Kazutaka; Kimura, Toshikiro
CORPORATE SOURCE: Department of Pharmaceutics, Faculty of Pharmaceutical Sciences, Okayama University, Tsushima-naka Okayama, Japan
SOURCE: Journal of Controlled Release (2004), 99(1), 63-71
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To develop the safe formulation that can safely improve bioavailability of poorly absorbable drugs and that is practically available, the authors prepared the suppositories of rebamipide, a poorly soluble and poorly absorbable antiulcer drug, by employing the combinatorial use of sodium laurate (C12), an absorption enhancer, with taurine (Tau) or L-glutamine (L-Gln), an adjuvant exerting the cytoprotective action. Although the dissoln. of rebamipide from fatty base (FB) suppository prepared using Witepsol H-15 was very slow, it was remarkably improved by the addition of C12 and L-Gln or Tau into the suppository. On the other hand, the dissoln. of rebamipide from water-soluble base (WB) suppository prepared using polyethylene glycol was very rapid and the addition of adjuvants did not

influence its dissoln. so much. Rectal absorption of rebamipide examined in rats was remarkably improved by FB suppository containing C12 or both C12 and Tau, while the enhancing effect of C12 was relatively small in the case of WB suppositories. Biochem. and histopathol. studies have confirmed that FB suppository containing both C12 and Tau or L-Gln did not cause any serious local damage, while FB suppository containing C12 only caused the erosion and shrinkage for a lot of rectal epithelial cells. In conclusion, FB suppository employing the combinatorial use of C12 with Tau could be a promising formulation that is effective and safe enough for poorly absorbable drugs to be practically administered.

IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(development of suppository formulation safely improving rectal absorption of rebamipide by sodium laurate and taurine or L-glutamine)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 142:16583 CA

TITLE: Pharmacological characterization of rebamipide: its cholecystokinin CCK1 receptor binding profile and effects on Ca2+ mobilization and amylase release in rat pancreatic acinar cells

AUTHOR(S): Moon, Seok Jun; An, Jeong Mi; Kim, Juyeon; Lee, Syng-Ill; Ahn, Wooin; Kim, Kyung Hwan; Seo, Jeong Taeg

CORPORATE SOURCE: Department of Oral Biology, Brain Korea 21 Project for Medical Sciences, Yonsei University College of Dentistry, Seoul, 120-752, S. Korea

SOURCE: European Journal of Pharmacology (2004), 505(1-3), 61-66
CODEN: EJPHAZ; ISSN: 0014-2999

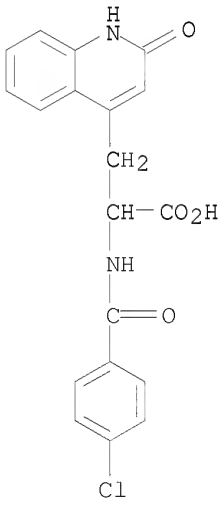
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors previously reported that rebamipide (2-(4-chlorobenzoylamino)-3-[2(1H)-quinolinon-4-yl]-propionic acid) generated oscillations of intracellular Ca2+ concentration ([Ca2+]i) probably through the activation of cholecystokinin type 1 (CCK1) receptors in rat pancreatic acinar cells. Therefore, in the present study, the authors aimed to establish the pharmacol. characteristics of rebamipide in rat pancreatic acinar cells. CCK-8S and rebamipide inhibited [125I]BH-CCK-8S binding to rat pancreatic acinar cell membranes with IC50 values of 3.13 nM and 37.7 μM, resp. CCK-8S usually evoked [Ca2+]i oscillations at concns. lower than 50 pM, and it induced biphasic [Ca2+]i increases at higher concns. In contrast to CCK-8S, rebamipide only induced [Ca2+]i oscillations at all the concns. the authors used in this study. In addition, rebamipide was shown to inhibit high concns. of CCK-8S-induced biphasic increases in [Ca2+]i, suggesting that rebamipide might be a partial agonist at cholecystokinin CCK1 receptors. Although rebamipide induced [Ca2+]i oscillations by activating the cholecystokinin CCK1 receptors, rebamipide did not cause amylase release and only inhibited CCK-stimulated amylase release reversibly and dose-dependently. However, rebamipide did not inhibit carbachol-, vasoactive intestinal polypeptide (VIP)-, and forskolin-induced amylase releases. These data indicate that rebamipide functions as a partial agonist for Ca2+-mobilizing action, and it is also an antagonist for the amylase-releasing action of CCK.

IT 90098-04-7, Rebamipide
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. characterization of rebamipide in relation to cholecystokinin CCK1 receptor binding profile and effects on Ca2+ mobilization and amylase release in rat pancreatic acinar cells)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS

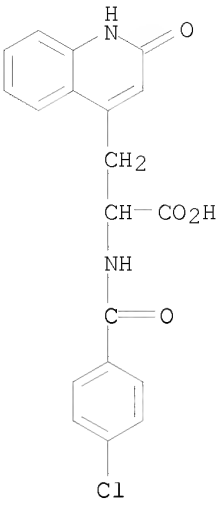
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 9 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 141:254186 CA
TITLE: Rebamipide Activates Genes Encoding Angiogenic Growth Factors and Cox2 and Stimulates Angiogenesis: A Key to Its Ulcer Healing Action?
AUTHOR(S): Tarnawski, A. S.; Chai, J.; Pai, R.; Chiou, S.-K.
CORPORATE SOURCE: The VA Medical Center, University of California, Irvine, CA, USA
SOURCE: Digestive Diseases and Sciences (2004), 49(2), 202-209
CODEN: DDSCDJ; ISSN: 0163-2116
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Clin. and exptl. data indicate that rebamipide accelerates ulcer healing, improves scar quality, and prevents ulcer recurrence. However, the mechanisms responsible for these rebamipides' actions are not fully elucidated. We studied, using gene expression microarray anal., which of the ulcer healing genes are activated by rebamipide treatment. Normal rat gastric epithelial cells (RGM1) were treated with either vehicle or rebamipide. Gene expression was determined using Affymetrix rat genome U34A gene chip arrays and data were analyzed using the GeneSpring program. Activation of some of the genes and protein translation were also examined by RT/PCR and Western blotting. Rebamipide significantly upregulated the proangiogenic genes encoding vascular endothelial growth factor (VEGF), by 7.5-fold, heparin binding epidermal growth-like factor (HB-EGF), by .apprx.5-fold, fibroblast growth factor receptor-2 (FGFR2), by 4.4-fold, and cyclooxygenase-2 (Cox2), by 9.3-fold, as well as growth promoting genes, e.g., insulin growth factor-1 (IGF-1), by 5-fold. RT/PCR and Western blotting demonstrated that Cox2 mRNA and protein were upregulated; the latter, .apprx.6-fold. Treatment of rat gastric mucosal endothelial cells with rebamipide stimulated in vitro angiogenesis by .apprx.240% (vs. controls, $P < 0.001$). Conclusions are as follows. (1) Rebamipide activates in gastric epithelial RGM-1 cells a genetic program that promotes angiogenesis and signals cell growth and tissue regeneration. (2) In addition, rebamipide treatment directly stimulates angiogenesis in gastric microvascular endothelial cells. Thus rebamipide has two sep. and distinct mechanisms of proangiogenic action: one through activation in gastric epithelial cells of proangiogenic growth factor genes and the second a direct angiogenic action on microvascular endothelial cells.

IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rebamipide activates in gastric epithelial cells of proangiogenic growth factor genes promoting angiogenesis and tissue regeneration and direct angiogenic action on microvascular endothelial cell in rat RGM1)

RN 90098-04-7 CA
CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

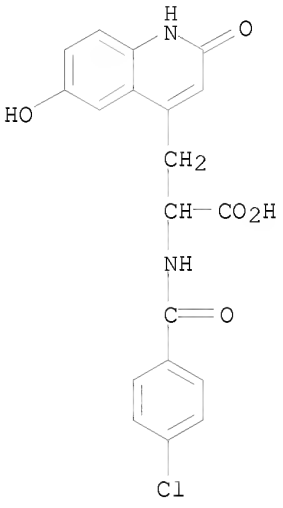
L15 ANSWER 10 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 141:199879 CA
TITLE: Mechanism of hydroxyl radical scavenging by rebamipide: Identification of mono-hydroxylated rebamipide as a major reaction product
AUTHOR(S): Sakurai, Kazushi; Sasabe, Hiroyuki; Koga, Toshihisa; Konishi, Tetsuya
CORPORATE SOURCE: Medical and Scientific Department, Pharmaceutical Marketing Division, Otsuka Pharmaceutical Co. Ltd, Tokyo, 101-8535, Japan
SOURCE: Free Radical Research (2004), 38(5), 487-494
CODEN: FRARER; ISSN: 1071-5762
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rebamipide, an antiulcer agent, is known as a potent hydroxyl radical (.OH) scavenger. In the present study, we further characterized the scavenging effect of rebamipide against .OH generated by UV irradiation of hydrogen peroxide (H2O2), and identified the reaction products to elucidate the mechanism of the reaction. Scavenging effect of rebamipide was accessed by ESR using DMPO as a .OH-trapping agent after UVB exposure (305 nm) to H2O2 for 1 min in the presence of rebamipide. The signal intensity of .OH adduct of DMPO (DMPO-OH) was markedly reduced by rebamipide in a concentration-dependent fashion as well as by DMSO and glutathione as reference radical scavengers. Their second order rate constant values were 5.62+1010, 8.16+109 and 1.65+1010 M-1 s-1, resp. As the rebamipide absorption spectrum disappeared during the reaction, a new spectrum grew due to generation of rather specific reaction product. The reaction product was characterized by LC-MS/MS and NMR measurements. Finally, a hydroxylated rebamipide at the 3-position of the 2(1H)-quinolinone nucleus was newly identified as the major product exclusively formed in the reaction between rebamipide and the .OH

generated by UVB/H2O2. Specific formation of this product explained the mol. characteristics of rebamipide as a potential .OH scavenger.

IT 90098-82-1, OPC 12959
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mechanism of hydroxyl radical scavenging by rebamipide and identification of mono-hydroxylated rebamipide as a major reaction product)

RN 90098-82-1 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-6-hydroxy-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 11 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 141:179660 CA

TITLE: Solvent systems containing PEG and surfactants for improvement of dissolution rate of hardly soluble drugs

INVENTOR(S): Kim, Jae-Hwan; Lee, Kyung-Sik; Shin, Woo-Choul; Lee, So-Ra; Yi, Jae-Hun

PATENT ASSIGNEE(S): R & P Korea Co., Ltd., S. Korea

SOURCE: U.S. Pat. Appl. Publ., 17 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040157928	A1	20040812	US 2003-682989	20031014 <--
KR 2004073255	A	20040819	KR 2003-60665	20030901 <--
WO 2004071490	A1	20040826	WO 2003-KR1833	20030905 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR,
TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

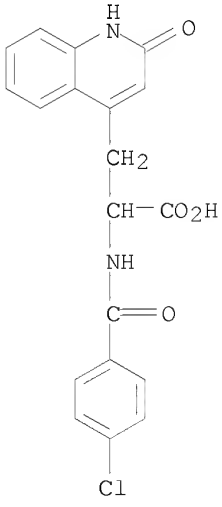
AU 2003261633	A1	20040906	AU 2003-261633	20030905 <--
EP 1605916	A1	20051221	EP 2003-815868	20030905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006514119	T	20060427	JP 2005-515721	20030905
PRIORITY APPLN. INFO.:			KR 2003-8931	A 20030212
			KR 2003-11056	A 20030221
			KR 2003-60665	A 20030901
			WO 2003-KR1833	W 20030905

AB The present invention relates to a solvent system with improved disintegration degree and dissoln. ratio of a hardly soluble drug by highly concentrating the drug through partial ionization, and by establishing optimal conditions for enhancing bioavailability of the drug, such as the co-relation between the acid drug and the accompanied components, ionization degree of a solvent system, use of an appropriate cation acceptance, water content, selection of optimal mixing ratio of the resp. components and use of specific surfactants, and to a pharmaceutical preparation comprising the same. The solvent system of the invention has advantages in that it can enhance bioavailability by improving the disintegration degree and dissoln. ratio of a hardly soluble drug and also provide a capsule with a sufficiently small volume to permit easy swallowing.

IT 90098-04-7, Rebamipide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solvent systems containing PEG and surfactants and cation acceptant mols. for improvement of dissoln. rate of hardly soluble drugs)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)

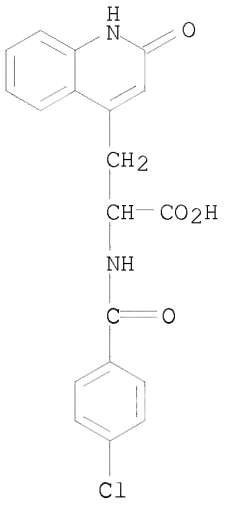


L15 ANSWER 12 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 141:46698 CA
TITLE: Determination of Rebamipide in Human Plasma by HPLC
AUTHOR(S): Jeoung, Min Kyo; Kim, Chang Soo; Kim, Nam Hee; Hong, Jin Tae; Chung, Youn-Bok; Park, Youmie; Kim, Kyoung Soon; Moon, Dong-Cheul
CORPORATE SOURCE: College of Pharmacy, Chungbuk National University, Cheongju, Heungduk Gu, S. Korea
SOURCE: Journal of Liquid Chromatography & Related Technologies (2004), 27(12), 1925-1935
CODEN: JLCTFC; ISSN: 1082-6076
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A simple determination method of rebamipide in human plasma by using high performance liquid chromatog. (HPLC) was developed. The method involves a single liquid-liquid extraction and reversed-phase chromatog. with fluorometric detection (excitation, 320 nm; emission, 380 nm). Analytes were extracted from plasma samples that contain an internal standard (ofloxacin) into ethylacetate with a high yield after adjustment to pH 2-3. Separation was accomplished at 60 on a reversed-phase column using a mobile phase of acetonitrile-water-acetic acid (30:70:5, volume/volume, pH 2.4), at a flow-rate of 1.0 mL/min. The linear range of the assay was 2-500 ng/mL of the drug in plasma and the limit of quantitation was 2.0 ng/mL. The intra- and inter-day relative standard deviation (RSD) were less than 10% and the accuracy of the assay was in the range of 97-104%. Anal. of the drug in human plasma indicates that the procedure can be carried out conveniently and quickly and, therefore, is suitable for obtaining pharmacokinetic profiles in human subjects after oral administration of different types of the drug.

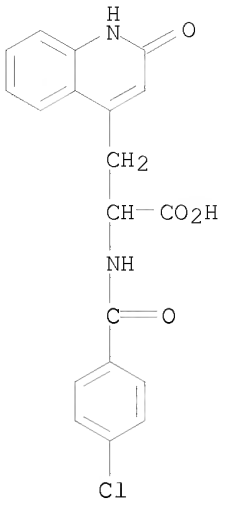
IT 90098-04-7, Rebamipide
RL: ANT (Analyte); PKT (Pharmacokinetics); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(determination of rebamipide in human plasma by HPLC)

RN 90098-04-7 CA
CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

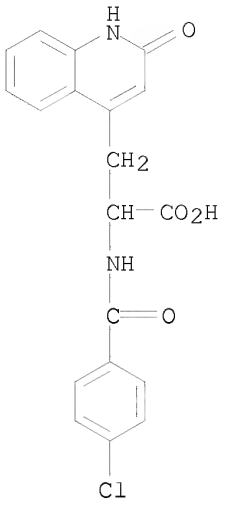
L15 ANSWER 13 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 141:16663 CA
TITLE: Effect of mucosal protective agents in urea breath test
AUTHOR(S): Higuchi, Kazuhide; Watanabe, Toshio; Shiba, Masatsugu; Tominaga, Kazunari; Fujiwara, Yasuhiro; Arakawa, Tetsuo
CORPORATE SOURCE: Graduate School of Medicine, Osaka Prefectural University, Japan
SOURCE: Helicobacter Research (2004), 8(1), 37-41
CODEN: HREEAQ; ISSN: 1342-4319
PUBLISHER: Sentan Igakusha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review. Effect of mucosal protective agents in urea breath test is reviewed including antibacterial activity of several cytoprotective antiulcer agents such as lansoprazole, famotidine, roxatidine and rebamipide against Helicobacter pylori, and their influence on the urea breath test for the diagnosis of Helicobacter pylori infection with examples.
IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of mucosal protective agents in urea breath test)
RN 90098-04-7 CA
CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



L15 ANSWER 14 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 141:12295 CA
TITLE: Tablets which rapidly disintegrate in the oral cavity
INVENTOR(S): Namiki, Noriyuki; Sasaki, Tadanori
PATENT ASSIGNEE(S): Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004155781	A	20040603	JP 2003-357803	20031017 <--
PRIORITY APPLN. INFO.:			JP 2002-302546 A	20021017

AB The tablets contain cocoa powder and pharmaceuticals having unpleasant taste. Preferably, the cocoa powder contains 10-24 weight% cacao butter. Tablets prepared from a composition containing rebamipide 10, cocoa powder 7, D-mannitol 257.4, and poly(vinylpyrrolidone) 5.6 g rapidly disintegrated in the oral cavity. The unpleasant taste of rebamipide was masked.
IT 90098-04-7, Rebamipide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rapidly disintegrating oral tablets containing cacao powder and sweeteners for masking of unpleasant taste of pharmaceuticals)
RN 90098-04-7 CA
CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



L15 ANSWER 15 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 141:337 CA
TITLE: Bioequivalence of rebamipide granules and tablets in healthy adult male volunteers
AUTHOR(S): Hasegawa, Setsuo; Sekino, Hisakuni; Matsuoka, Osamu; Saito, Kazunori; Sekino, Hisayuki; Morikawa, Aki; Uchida, Kaya; Koike, Masami; Azuma, Junichi
CORPORATE SOURCE: Sekino Clinical Pharmacology Clinic, Tokyo, Japan
SOURCE: Clinical Drug Investigation (2003), 23(12), 771-779
CODEN: CDINFR; ISSN: 1173-2563
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

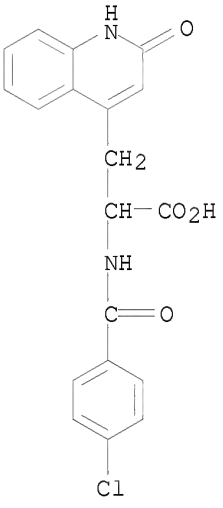
AB Rebamipide tablets, which are used in the treatment of patients with gastric ulcers or gastritis, can be difficult to administer in subjects with reduced swallowing ability or impaired swallowing. The granule formulation may be more easily administered in these patients. The bioequivalence between rebamipide granules (20%/0.5g) and tablets (100mg) was determined in healthy male adult volunteers, in accordance with the Partially Revised Guidelines for Bioequivalence Studies of Generic Products. In a randomized, nonblind, crossover design, 28 individuals were allocated into two groups of 14 to receive either rebamipide granules or rebamipide tablets. Each individual, under fasting conditions, was administered a single oral dose of rebamipide 100mg followed by a 7-day washout period. Individuals then received a single oral dose of the other rebamipide formulation. Blood samples were collected at 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12 and 24 h. Plasma rebamipide concns. were measured by validated high-performance liquid chromatog. with tandem mass spectrometry. The plasma concentration-time profiles and pharmacokinetic parameters of rebamipide after administration of the granule formulation were similar to those of the tablet in 27 healthy male volunteers. Following administration of the granule formulation, the area under the plasma concentration-time curve from time 0-24 h (AUC24h) was 912.82 μg/L • h,

the maximum plasma concentration (Cmax) was 241.82 μg/L, time to maximum plasma concentration (tmax) was 2.5 h, and plasma elimination half-life (t1/2) was 1.97 h. Corresponding values for the tablet formulation were 873.55 μg/L • h, 216.19 μg/L, 2.4 h, and 1.94 h. The difference in mean log values was 1.01 for AUC24h and 1.09 for Cmax after granule and tablet administration. The 90% confidence interval of this difference in mean log value was 0.93-1.10 for AUC24h, and 0.97-1.21 for Cmax. This satisfies the criteria for bioequivalence in the guidelines [within log (0.8) to log (1.25)]. Rebamipide granules (20%/0.5g) and tablet (100mg) were bioequivalent. Rebamipide granules may therefore be a more practical treatment option in patients with gastric ulcers or gastritis who have difficulty swallowing tablets.

IT 90098-04-7, Rebamipide
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioequivalence of rebamipide granules and tablets in healthy adult male volunteers)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 16 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 140:357217 CA

TITLE: Improved preparation of rebamipide

INVENTOR(S): Moon, Yang Ho; Ha, Tae Eui; Kim, Hong Sun; Lee, Jae Chul; Lee, Seung Chul; Chang, Young Gil; Lee, Kwan Joo

PATENT ASSIGNEE(S): Hanmi Farm Co., Ltd., S. Korea

SOURCE: Jpn. Kokai Tokkyo Koho, 15 pp.
CODEN: JKXXAF

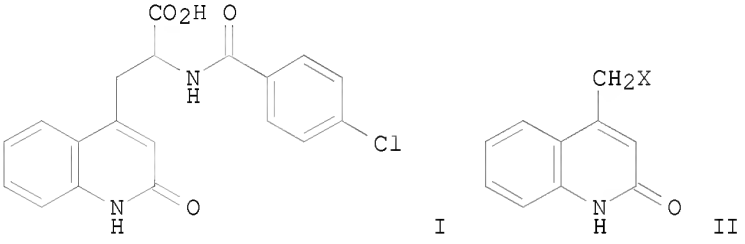
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004131506	A	20040430	JP 2003-353221	20031014 <--
JP 4095010	B2	20080604		
KR 2004033145	A	20040421	KR 2002-62058	20021011 <--

PRIORITY APPLN. INFO.: KR 2002-62058 A 20021011
GI



I

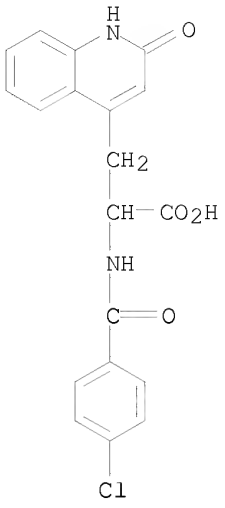
II

AB Rebamipide (I) is prepared from 4-(halomethyl)carbostyryl II (X = Cl, Br, iodine) and AcNHCH(CO2Et)2 via II (X = AcNHCHCO2H) and II.HCl (X = NH2CHCO2H). Thus, refluxing II (X = Br) with AcNHCH(CO2Et)2 and EtONa in EtOH for 2 h, further refluxed with aqueous KOH for 3 h, and acidified to give 98% II (X = AcNHCHCO2H), which was refluxed with AcOH and concentrated HCl for 3 h to afford 96% II.HCl (X = NH2CHCO2H). Amidation of the product with 4-chlorobenzoyl chloride gave 93% I.

IT 90098-04-7P, Rebamipide
RL: IMF (Industrial manufacture); PREP (Preparation)
(improved preparation of rebamipide from (halomethyl)carbostyryl and acetamidomalonate)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



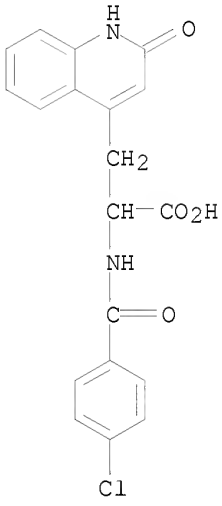
L15 ANSWER 17 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 140:297227 CA
TITLE: Influence of anti-ulcer drugs used in Japan on the result of 13C-urea breath test for the diagnosis of Helicobacter pylori infection
AUTHOR(S): Murakami, Kazunari; Sato, Ryugo; Okimoto, Tadayoshi; Watanabe, Koichiro; Nasu, Masaru; Fujioka, Toshio; Kodama, Masaaki; Kagawa, Jiro
CORPORATE SOURCE: Second Department of Internal Medicine, Oita Medical University, Oita, 879-5593, Japan
SOURCE: Journal of Gastroenterology (2003), 38(10), 937-941
CODEN: JOGAET; ISSN: 0944-1174
PUBLISHER: Springer-Verlag Tokyo
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 13C-urea breath test (UBT) is a simple test for the diagnosis of Helicobacter pylori infection, but several factors have been reported to affect the results of this test. In this study, the effects of the anti-ulcer drugs used in Japan on the results of the UBT were determined The subjects of the study were 64 adult volunteers who tested pos. for H. pylori infection by the serum antibody method. Eight classes of anti-ulcer drugs used in Japan were administered at their usual doses to these subjects: lansoprazole, a proton pump inhibitor (PPI); nizatidine, an H2-receptor antagonist (H2RA); and polaprezinc, ecabet sodium, rebamipide, teprenone, cetraxate hydrochloride, and sucralfate, all mucoprotective agents. The study drugs were randomized for administration to the subjects, and each of the drugs was administered for 14 consecutive days. The UBT was performed on days 0, 14, and 21. The mean Δ13C.permill. in the lansoprazole group was significantly decreased on day 14, to below 10.permill., in 4 of 16 subjects, and in 1 of the 4 subjects, the test result was neg., with the Δ13C.permill. falling to 1.7.permill.. The value returned to baseline 1 wk after the discontinuation of lansoprazole. The other drugs administered had no

significant effect on the result of the UBT, except that the mean Δ13C.permill. showed a tendency to decrease after the administration of ecabet sodium and rebamipide. Administration of a PPI may produce a false-neg. UBT result, while other anti-ulcer drugs, for the most part, have little effect on the result of the UBT when used alone.

IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-ulcer drugs effect on 13C-urea breath test result for diagnosis of Helicobacter pylori infection)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 18 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 140:281008 CA

TITLE: Preoperative administration of rebamipide significantly lowers body temperature and circulating interleukin-6 in gastric cancer patients after gastrectomy

AUTHOR(S): Shimada, S.; Inoue, K.; Kuramoto, M.; Suzuki, S.; Yamamoto, K.; Ogawa, M.

CORPORATE SOURCE: Department of Surgery II, Kumamoto University School of Medicine, Kumamoto, Japan

SOURCE: Digestive Surgery (2003), 20(6), 500-505
CODEN: DSIUAN; ISSN: 0253-4886

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

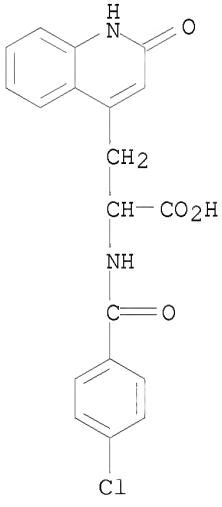
LANGUAGE: English

AB It has recently been reported that rebamipide (OPC-12759) inhibits inflammatory cytokines and activation of neutrophils. The aim of the present study was to investigate the effects of preoperative administration of rebamipide on parameters of systemic inflammatory

response syndrome (SIRS) and serum levels of inflammatory cytokines in gastric cancer patients after gastrectomy. We measured the parameters of SIRS, circulating cytokines and acute phase reactants in patients after (i) distal gastrectomy with D2 lymph node dissection (group 1, n = 10); (ii) distal gastrectomy with D2 lymph node dissection following administration of rebamipide (group 2, n = 10), and (iii) laparoscopy-assisted distal gastrectomy (LADG) with D1 lymph node dissection (group 3, n = 10). Group 2 was administered 100 mg of rebamipide 3 times/day after meals for 7 days before surgery. Among the parameters of SIRS, a difference was observed in body temperature on day 3. The mean body temperature of group 2 was significantly lower than group 1 ($p = 0.006$), and was similar to group 3. In proinflammatory cytokines, a significant difference was observed in the serum levels of interleukin (IL)-6. On day 1 the IL-6 levels of group 2 were significantly lower than those of group 1 ($p < 0.001$). The changes in the IL-6 level of group 2 were similar to group 3, except in the very early postoperative phase. However, other proinflammatory cytokines, such as IL-8 and IL-10, were not detected, and there was no difference in C-reactive protein between the 3 groups. Preoperative administration of rebamipide significantly decreased postoperative body temps. and circulating IL-6 in gastric cancer patients after gastrectomy to levels similar to those of patients with LADG.

IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of rebamipide preoperative administration on body temperature and interleukin-6 in gastric cancer patients after gastrectomy)

RN 90098-04-7 CA
CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 19 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 140:246945 CA

TITLE: Free radical scavenger effect of rebamipide in sperm processing and cryopreservation

AUTHOR(S): Park, Nam Cheol; Park, Hyun Jun; Lee, Kyeong Mi; Shin, Dong Gil

CORPORATE SOURCE: Department of Urology, College of Medicine, Pusan National University, Pusan, 602 739, S. Korea

SOURCE: Asian Journal of Andrology (2003), 5(3), 195-201
CODEN: ASJAF8; ISSN: 1008-682X

PUBLISHER: Science Press

DOCUMENT TYPE: Journal

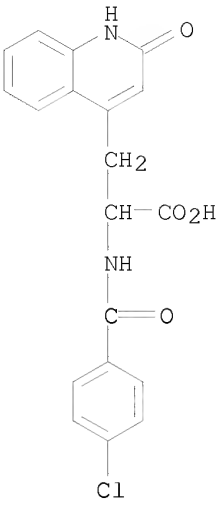
LANGUAGE: English

AB Aim: To study the effect of rebamipide added to semen samples and cryoprotectant on reactive oxygen species (ROS) production Methods: Semen samples from 30 fertile and healthy volunteers were collected by masturbation after 2 days .apprx. 3 days of abstinence. After liquefaction, the specimens were diluted with sperm wash media to a uniform d. of 20+106/mL. Rebamipide was added to semen samples and cryoprotectant to a final concentration of 10 μmol/L, 30 μmol/L, 100 μmol/L or 300 μmol/L. Specimens were incubated at 37° in a 0.5 % CO2 incubator for 1 h or cryopreserved at -196° LN2 for 3 days. The sperm motility and viability and the levels of ROS and lipid peroxidn. of sperm membranae were assessed before and after incubation and cryopreservation by means of computer assisted semen analyzer, eosin-nigrosin stain, chemiluminescence and thiobarbituric acid assay, resp. Results: The sperm motility was significantly increased after incubation with 100 μmol/L and 300 μmol/L rebamipide ($P<0.05$). After cryopreservation, the sperm motility was significantly decreased in all concns. ($P<0.05$), but the decrease was less with 100 μmol/L and 300 μmol/L rebamipide than that with other concns. The sperm viability showed no significant difference before and after incubation ($P>0.05$). The levels of ROS and lipid peroxidn. in semen were significantly decreased in proportion to the concns. of rebamipide both after incubation and cryopreservation ($P<0.05$). Conclusion: Rebamipide is an effective free radical scavenger in semen in vitro.

IT 90098-04-7, Rebamipide
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(free radical scavenger effect of rebamipide in sperm processing and cryopreservation)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 20 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 140:246152 CA
TITLE: Study of inhibition of CYP2A6 by some drugs derived from quinoline
AUTHOR(S): Hirano, Yoshie; Mizutani, Takaharu
CORPORATE SOURCE: Department of Drug Metabolism and Disposition, Graduate School of Pharmaceutical Sciences, Nagoya City University, Nagoya, 467-8603, Japan
SOURCE: Journal of Pharmacy and Pharmacology (2003), 55(12), 1667-1672
CODEN: JPPMAB; ISSN: 0022-3573
PUBLISHER: Pharmaceutical Press
DOCUMENT TYPE: Journal
LANGUAGE: English

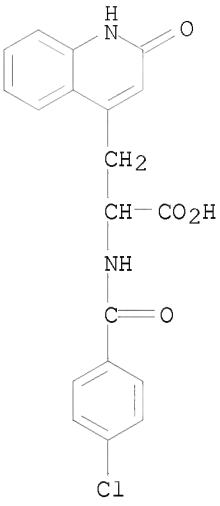
AB CYP2A6 metabolizes coumarin to 7-hydroxycoumarin showing fluorescence, as measured by fluorometry. Firstly, we measured the inhibition of coumarin 7-hydroxylase of cDNA-expressed human CYP2A6 and in bovine liver microsomes, by quinoline and fluoroquinolines (FQ). Quinoline, 5-FQ, 6-FQ and 8-FQ inhibited activity but 3-FQ showed little inhibition. This suggests that the position 3 of quinoline is a recognition site for CYP2A6. We found similar patterns of coumarin 7-hydroxylase activity with human pooled liver microsomes. The level of CYP2A6 in human and bovine microsomes is the same as that detected by immunol. titration with monoclonal antibody against CYP2A6. Secondly, we studied the inhibition of CYP2A6 with clin. used drugs of quinoline compds., such as norfloxacin as an antibacterial agent, quinidine as an antiarrhythmic agent, quinine and chloroquine as antimalaria agents and rebamipide as an anti-ulcer agent. IC50 values (concentration producing 50% inhibition in activity) of norfloxacin, rebamipide and chloroquine at mM concns. showed them to possess almost no inhibitory activity or influence on drug interaction. Meanwhile, the IC50 value of quinidine was 1.12 mM. The IC50 value of quinine was 160 μM

with weak inhibition, suggesting that quinine, at a high dose, influences the metabolism of substrates for CYP2A6 by drug-drug interaction. These results also show that CYP2A6 discriminates the structure difference between the diastereoisomers quinidine and quinine.

IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); BIOL (Biological study)
(inhibition of CYP2A6 by some drugs derived from quinoline)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 21 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 140:104929 CA

TITLE: Effects of antioxidative agents on apoptosis induced by ischaemia-reperfusion in rat intestinal mucosa

AUTHOR(S): Kojima, M.; Iwakiri, R.; Wu, B.; Fujise, T.; Watanabe, K.; Lin, T.; Amemori, S.; Sakata, H.; Shimoda, R.; Oguzu, T.; Ootani, A.; Tsunada, S.; Fujimoto, K.

CORPORATE SOURCE: Department of Internal Medicine and Gastrointestinal Endoscopy, Saga Medical School, Saga, 849-8501, Japan

SOURCE: Alimentary Pharmacology and Therapeutics (2003), 18(Suppl. 1), 139-145
CODEN: APTHEN; ISSN: 0269-2813

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

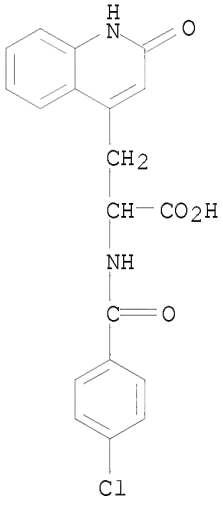
AB We have previously demonstrated that ischemia-reperfusion induces apoptosis in the intestinal mucosa. To evaluate that reactive oxygen species enhanced intestinal apoptosis after ischemia-reperfusion, we examined whether antioxidants reduced apoptosis. Rats were infused through a duodenal tube with antioxidative agents, glutathione, rebamipide and dimethylsulfoxide during 2 h before an ischemic insult. The superior mesenteric artery was occluded for 60 min. followed by 60 min.

reperfusion. Apoptosis was evaluated by percentage fragmented DNA (fragmented DNA/total DNA) and immunochem. staining. Increase in apoptosis in the intestinal mucosa after ischemia-reperfusion was attenuated by intraduodenal infusion of antioxidative agents, but was not completely abolished. Scavenging effects of the antioxidative agents attenuated increases in intestinal apoptosis, indicating that oxidative stress after ischemia-reperfusion plays an important role in induction of apoptosis in the intestinal mucosa.

IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of antioxidants on apoptosis induced by ischemia-reperfusion in rat intestinal mucosa)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 22 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 140:104928 CA

TITLE: The protective effect of rebamipide on paracellular permeability of rat gastric epithelial cells

AUTHOR(S): Joh, T.; Takezono, Y.; Oshima, T.; Sasaki, M.; Seno, K.; Yokoyama, Y.; Ohara, H.; Nomura, T.; Alexander, J. S.; Itoh, M.

CORPORATE SOURCE: Department of Internal Medicine & Bioregulation, Nagoya City University Graduate School of Medical Sciences, Nagoya, 467-8601, Japan

SOURCE: Alimentary Pharmacology and Therapeutics (2003), 18(Suppl. 1), 133-138
CODEN: APTHEN; ISSN: 0269-2813

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

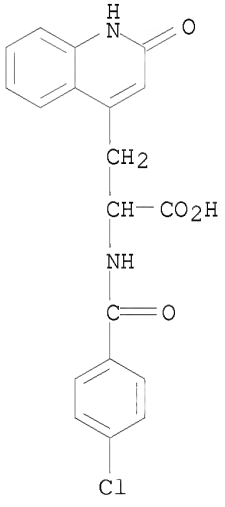
LANGUAGE: English

AB Barrier function in gastric epithelial cells is essential for the gastric defense mechanism against acid back-diffusion into the mucosal layer. Our previous study indicated that trans-epithelial resistance (TER) of rat gastric epithelial cells was rapidly increased when the cells were exposed to acid. This response to acid was diminished by indomethacin. The objective of this study was to evaluate the effects of a mucoprotective agent, rebamipide, on the non-steroidal antiinflammatory drug (NSAID)-induced increase of gastric epithelial permeability. Rat gastric epithelial cells were plated on tissue culture inserts. Cells were exposed to a NSAID (indomethacin, 10-7 M). Trans-epithelial permeability was measured by TER and diffusion rate of 14C-mannitol. The effect of rebamipide was evaluated by measuring TER. Endogenous prostaglandin E2 (PGE2) production in culture medium was also measured. Indomethacin gradually and significantly decreased TER and increased 14C-mannitol permeability. Rebamipide reversed the indomethacin-induced changes in epithelial permeability and induced PGE2 synthesis. This induction was blocked by either indomethacin or a cyclooxygenase (COX)-2 specific inhibitor. Thus, COX inhibitors such as indomethacin inhibit regulation of epithelial permeability by reducing PGE2. COX-1 has an important role in the gastric defense mechanism. Rebamipide suppressed an indomethacin-induced increase in gastric epithelial permeability by increasing PGE2 levels in a COX-2 dependent manner.

IT 90098-04-7, Rebamipide
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protective effect of rebamipide on paracellular permeability of rat gastric epithelial cells induced by COX inhibitors)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 23 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 140:104927 CA

TITLE: Expression of midkine and receptor-like protein tyrosine phosphatase (RPTP)-β genes in the rat stomach and the influence of rebamipide

AUTHOR(S): Yuki, T.; Ishihara, S.; Rumi, M.; Cesar, F. Ortega-Cava; Kadowaki, Y.; Kazumori, H.; Yuki, M.; Wada, T.; Miyaoka, Y.; Yoshino, N.; Kinoshita, Y.

CORPORATE SOURCE: Department of Internal Medicine II, Shimane Medical University, Shimane, Japan

SOURCE: Alimentary Pharmacology and Therapeutics (2003), 18(Suppl. 1), 106-112
CODEN: APTHEN; ISSN: 0269-2813

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

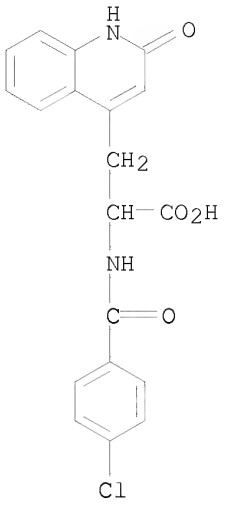
LANGUAGE: English

AB Midkine has been reported to bind to receptor-like protein tyrosine phosphatase (RPTP)-β and to play important roles in growth and differentiation of various cells. Midkine is expressed in rat stomach during exptl. ulcer healing, suggesting that the midkine-RPTP-β system has some physiol. functions in the stomach. Rebamipide is a mucoprotective drug used for the treatment of gastric ulcers. We have tested the hypothesis that the ulcer healing mechanism stimulated by rebamipide is linked physiol. to the gastric midkine-RPTP-β system. Seven-week-old-male Wistar rats were used. Midkine and RPTP-β gene expression in rat stomach was investigated by laser capture microdissection coupled with the reverse transcription-polymerase chain reaction (RT-PCR). The effects of rebamipide on midkine and RPTP-β expression in rat stomach and the gastric epithelial cell line RGM1 were evaluated by RT-PCR and Northern blot analyses. Midkine and RPTP-β expression was detected in the gastric mucosal, submucosal and muscle layers. Rebamipide stimulated both midkine and RPTP-β expression in rat stomach and RGM1 cells. Thus, rebamipide may protect the gastric mucosa by regulating midkine and RPTP-β expression.

IT 90098-04-7, Rebamipide
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(expression of midkine and receptor-like protein tyrosine phosphatase (RPTP)-β genes in the rat stomach and the influence of rebamipide)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

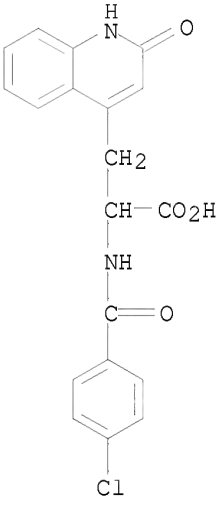
L15 ANSWER 24 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 140:104926 CA
TITLE: Interaction of leptin with gastric myofibroblast transdifferentiation in Helicobacter pylori-infected Mongolian gerbils: the effect of rebamipide
AUTHOR(S): Nakamura, M.; Akiba, Y.; Matsui, H.; Tsuchimoto, K.; Ishii, H.
CORPORATE SOURCE: Center for Basic Research, Kitasato Institute, Tokyo, 108-8642, Japan
SOURCE: Alimentary Pharmacology and Therapeutics (2003), 18(Suppl. 1), 99-105
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Our recent histochem. studies have revealed the marked increase of myofibroblasts in the Helicobacter pylori-infected Mongolian gerbil fundic mucosa, while the mediators, which facilitate the conversion of fibroblasts to the myofibroblasts remain unknown. The present study was undertaken to clarify the alteration of leptin in the control and H. pylori-infected Mongolian gerbil stomach. The effector sites of rebamipide were also investigated in relation to leptin. The localization of leptin was investigated by the indirect immunofluorescence. Plasma leptin levels were determined by ELISA method. The localization of 3H-rebamipide binding sites was investigated by autoradiog. Serum leptin content in H. pylori-infected Mongolian gerbils was significantly increased. The presence of leptin immunoreactivity was recognized in the endothelial cells of the microcirculatory network and very weakly in the glandular cells in the control group, while in the H. pylori-infected group leptin was markedly recognized in the mesenchymal cells. Rebamipide bound to the fibroblasts and surface mucous cells and decreased the leptin immunoreactivity in the gastric mucosa. Leptin was mostly found in the

mesenchymal cells. Rebamipide administration brought about the decrease of leptin in the gastric mucosa of the H. pylori-infected gerbils.

IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(interaction of leptin with gastric myofibroblast transdifferentiation in Helicobacter pylori-infected Mongolian gerbils and the effect of rebamipide)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 25 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 140:104925 CA

TITLE: Rebamipide binds to iNOS-positive cells in acetic acid-treated but not in ethanol-treated rat gastric mucosa

AUTHOR(S): Nakamura, M.; Akiba, Y.; Matsui, H.; Tsuchimoto, K.; Ishii, H.

CORPORATE SOURCE: Center for Basic Research, Kitasato Institute, Minato-ku, Tokyo, 108-8642, Japan

SOURCE: Alimentary Pharmacology and Therapeutics (2003), 18(Suppl. 1), 76-81
CODEN: APTHEN; ISSN: 0269-2813

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

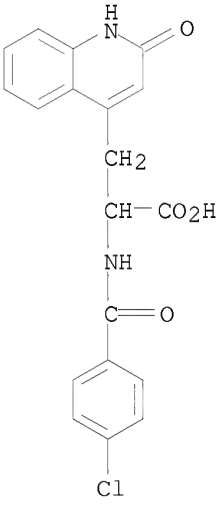
AB Rebamipide is a gastroprotective agent to stimulate prostaglandin generation in gastric mucosa and attenuate the activity of neutrophils, but direct evidence for the effector sites of this agent has remained to be clarified. The present study was undertaken to show the effector sites of rebamipide in control and ulcer-provoked rats. The rats were divided into control, acetic acid- and ethanol-treated rats. In the acetic

acid-treated group, 100% acetic acid was attached to the serosal surface of the stomach for 30 s, 7 days before the expts. In the ethanol-treated group, a dose of 0.5 mL/100 g body weight of 50% ethanol was administered through orogastric intubation 2 h before the expts. Using the unfixed cryostat sections, aqueous solution of 3H-rebamipide was applied and the localization of the binding sites of rebamipide was investigated by autoradiog. In the control rats, rebamipide was found to bind to the surface epithelial cells. In the ethanol-treated group, few binding sites were observed in the damaged gastric mucosa. In the acetic acid-treated group, the marked accumulation of the binding sites of 3H-rebamipide was observed in the mesenchymal cells in the lamina propria mucosae between the regenerated gastric epithelial cells. Combination of autoradiog. and immunohistochem. has revealed that iNOS-immunoreactive cells showed strong binding of rebamipide in the acetic acid-treated group. Some of these cells were CD68-pos. macrophages, while others were CD68-neg., corresponding to polymorphonuclear leukocytes. In the ethanol-treated acute gastric mucosal injury group, few binding sites were observed in the damaged gastric mucosa. Thus, autoradiog. has made it clear that rebamipide binds to iNOS-pos. cells in the gastric mucosa 7 days after acetic acid-treatment.

IT 90098-04-7, Rebamipide
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rebamipide binds to iNOS-pos. cells in acetic acid-treated but not in ethanol-treated rat gastric mucosa)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 26 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 140:104924 CA

TITLE: The effect of rebamipide on Helicobacter pylori extract-mediated changes of gene expression in gastric

epithelial cells

AUTHOR(S): Yoshida, N.; Ishikawa, T.; Ichiishi, E.; Yoshida, Y.; Hanashiro, K.; Kuchide, M.; Uchiyama, K.; Kokura, S.; Ichikawa, H.; Naito, Y.; Yamamura, Y.; Okanoue, T.; Yoshikawa, T.

CORPORATE SOURCE: Molecular Gastroenterology and Hepatology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, 602-8566, Japan

SOURCE: Alimentary Pharmacology and Therapeutics (2003), 18(Suppl. 1), 63-75
CODEN: APTHEN; ISSN: 0269-2813

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

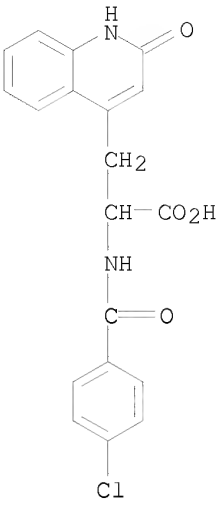
LANGUAGE: English

AB Recent studies have shown that Helicobacter pylori affects intracellular signal transduction in host cells, leading to the activation of transcriptional factors and the induction of pro-inflammatory cytokines. On the other hand, rebamipide, an anti-gastritis and anti-ulcer agent, could scavenge reactive oxygen species and reduce interleukin-8 (IL-8) expression in gastric epithelial cells induced by H. pylori-stimulation through the attenuated activation of nuclear factor-κB (NF-κB). In this study, we investigated the effects of rebamipide on gene expression in H. pylori-stimulated epithelial cells using DNA chip technol. H. pylori water extract (HPE) was prepared from NCTC11637, the type strain of H. pylori. Total RNA was extracted from MKN45 cells, a human gastric cancer cell line, following HPE-stimulation with and without rebamipide for 3 h, and differences in gene expression profiles were observed using GeneChip and Human 6800 probe array. The GeneChip anal. demonstrated that 132 up-regulated genes and 873 down-regulated genes, such as growth factors, chemokines and transcription factors, were detected in MKN45 cells 3 h after stimulation of H. pylori. Among them, several genes, including bFGF, RANTES and MIP-2β, were previously unknown to be expressed in H. pylori-stimulated human gastric cells. Rebamipide reduced expression of 119 genes encoding cytokines, growth factors and their receptors and transcription factors. These findings suggest that rebamipide could inhibit inflammatory reactions and tumor progression by modifying H. pylori infection-induced gene expression in gastric epithelial cells.

IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of rebamipide on Helicobacter pylori extract-mediated changes of gene expression in gastric epithelial cells)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

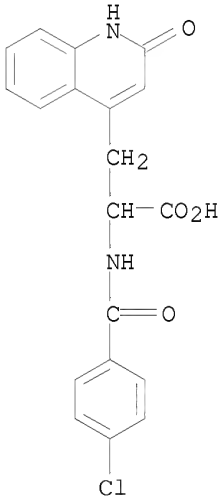
L15 ANSWER 27 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 140:104923 CA
TITLE: Effect of long-term administration of rebamipide on Helicobacter pylori infection in mice
AUTHOR(S): Hahm, K. B.; Kim, D. H.; Lee, K. M.; Lee, J. S.; Surh, Y. J.; Kim, Y. B.; Yoo, B. M.; Kim, J. H.; Joo, H. J.; Cho, Y. K.; Nam, K. T.; Cho, S. W.
CORPORATE SOURCE: Genomic Research Center for Gastroenterology, Ajou Helicobacter Research Group, Ajou University School of Medicine, Suwon, 442-749, S. Korea
SOURCE: Alimentary Pharmacology and Therapeutics (2003), 18(Suppl. 1), 24-38
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It has been suggested that chronic, persistent, uncontrolled inflammation in the stomach could provide the basic step for the beginning of carcinogenesis. One of the potential clin. applications of rebamipide is the inhibition of the immunoinflammatory response in gastric mucosa imposed by Helicobacter pylori. In order to determine the implications of long-term rebamipide treatment in H. pylori infection, we studied the underlying moleculo-pathol. changes in gastric lesions in mice infected with H. pylori (SS1 strain), following this treatment. C57BL/6 mice were sacrificed 24 and 50 wk after H. pylori infection, resp. Colonization rates of H. pylori, degree of gastric inflammation and other pathol. changes including atrophic gastritis and metaplasia, serum levels of IL-1β, TNF-α, IFN-γ and IL-10, mRNA transcripts of various mouse cytokines and chemokines, and NF-κB binding activities, and finally the presence of gastric adenocarcinoma were compared between an H. pylori-infected group (HP), and an H. pylori-infected group administered with long-term rebamipide-containing pellet

diets (HPR). Serum levels of IL-1β, IFN-γ and TNF-α, the gastric mucosal expression of ICAM-1, HCAM and MMP, and transcriptional regulation of NF-κB-DNA binding were all significantly decreased in the HPR group compared with the HP group. An RNase protection assay showed, in the rebamipide administered group, significantly decreased mRNA levels of apoptosis-related genes such as caspase-8, FasL, Fas, TRAIL and various cytokine genes such as IFN-γ, RANTES, TNF-α, TNFR p75, IL-1β. In the experiment designed to provoke gastric cancer through MNU treatment with H. pylori infection, the incidence of gastric carcinoma was not different in either group. However, long-term administration of rebamipide showed the advantage of decreasing precancerous lesions like chronic atrophic gastritis and showed mol. evidence of attenuation of proliferation. Thus, the long-term administration of rebamipide should be considered in the treatment of H. pylori since it demonstrated mol. and biol. advantages like a lessening of gastric inflammation and a possible chemopreventive effect.

IT 90098-04-7, Rebamipide
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of long-term administration of rebamipide on Helicobacter pylori infection in mice and associated gastric inflammation and adenocarcinoma development)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

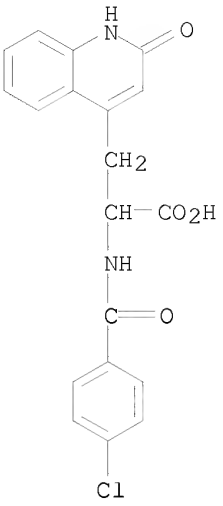
L15 ANSWER 28 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 140:104922 CA

TITLE: Comparison of the effects of rebamipide with those of cimetidine on chronic gastritis associated with Helicobacter pylori in Mongolian gerbils

AUTHOR(S): Higuchi, K.; Tanigawa, T.; Hamaguchi, M.; Takashima, T.; Sasaki, E.; Shiba, M.; Tominaga, K.; Fujiwara, Y.;

Oshitani, N.; Matsumoto, T.; Watanabe, T.; Arakawa, T.
CORPORATE SOURCE: Department of Gastroenterology, Osaka City University Graduate School of Medicine, Osaka, 545-8585, Japan
SOURCE: Alimentary Pharmacology and Therapeutics (2003), 18(Suppl. 1), 1-7
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of rebamipide on chronic gastritis associated with Helicobacter pylori have not been well-defined. We compared these effects of rebamipide with those of cimetidine in Mongolian gerbils infected with H. pylori. Mongolian gerbils with or without H. pylori were divided into 10 groups 6 wk after inoculation and fed diets containing a drug (rebamipide or cimetidine) or control diet. All animals were sacrificed 4 wk after grouping. Their stomachs were examined for histol., colonization by H. pylori, myeloperoxidase activity, production of neutrophil chemokine (CINC/KC) and tumor necrosis factor-α (TNF-α), and serum gastrin levels. H. pylori colonized all of the inoculated animals. Neither rebamipide nor cimetidine decreased myeloperoxidase activity, but each reduced wet stomach weight in H. pylori-infected animals. The amount of increase in CINC/KC and TNF-α in gastric tissue caused by H. pylori infection was decreased by treatment with rebamipide or cimetidine. H. pylori infection increased serum gastrin levels, and this increase was significantly enhanced by cimetidine but not rebamipide. Thus, rebamipide may improve H. pylori-infected chronic gastritis by preventing the production of inflammatory cytokines and chemokines, as does cimetidine, but may be preferable to cimetidine for long-term administration for treatment of H. pylori-infected chronic gastritis due to its effect on serum gastrin levels.
IT 90098-04-7, Rebamipide
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of the effects of rebamipide with those of cimetidine on chronic gastritis associated with Helicobacter pylori in Mongolian gerbils)
RN 90098-04-7 CA
CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

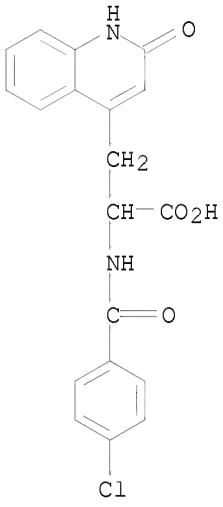
L15 ANSWER 29 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 140:104746 CA
TITLE: Effect of rebamipide on prostaglandin receptors-mediated increase of inflammatory cytokine production by macrophages
AUTHOR(S): Bamba, H.; Ota, S.; Kato, A.; Miyatani, H.; Kawamoto, C.; Yoshida, Y.; Fujiwara, K.
CORPORATE SOURCE: First Department of Internal Medicine, Saitama Medical Center, Saitama Medical School, Saitama, 350-8550, Japan
SOURCE: Alimentary Pharmacology and Therapeutics (2003), 18(Suppl. 1), 113-118
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rebamipide (Reb) is an anti-ulcer drug, and has unique properties such as antiinflammatory action. We previously reported that prostaglandins (PGs) dramatically increased vascular endothelial growth factor (VEGF), a known angiogenic factor and a vascular permeable factor, by activated macrophages through specific PGE receptor and peroxisome proliferator-activated receptor γ (PPARγ, a nuclear receptor of PG) mediated process. Effects of PGs on the production of other cytokines such as interleukin (IL)-6 and IL-8 have been controversial. In order to clarify the antiinflammatory roles of Reb, we examined the effect of Reb on PGE1- and 15-deoxy-Δ12,14-PGJ2 (a potent PPARγ ligand, 15d-PGJ2)-induced increase of VEGF production by macrophages. Addnl., effects of these PGs on the production of IL-6 and IL-8, and modulation of these actions by Reb were studied. Phorbol 12-myristate 13-acetate-differentiated U937 cells were used as a human macrophage model (H-Mac). VEGF, IL-6, IL-8 and cAMP were measured by EIA. Reb suppressed PGE1-, but not 15d-PGJ2-induced, increase of VEGF production partially through

decrease of cAMP formation. Reb suppressed PGE1-, but not 15d-PGJ2-induced increase of IL-6 and IL-8 production Thus, Reb suppresses membrane, but not nuclear PG receptor-mediated increase of inflammatory cytokine production, which may be involved in anti-ulcer action of this drug.

IT 90098-04-7, Rebamipide
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of rebamipide on prostaglandin receptor-mediated increase of inflammatory cytokine production by macrophages)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 30 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 140:104745 CA

TITLE: The effect of rebamipide on the expression of proinflammatory mediators and apoptosis in human neutrophils by Helicobacter pylori water-soluble surface proteins

AUTHOR(S): Kim, J. S.; Kim, J. M.; Jung, H. C.; Song, I. S.

CORPORATE SOURCE: Department of Internal Medicine, Liver Research Institute and Clinical Research Institute, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, 110-744, S. Korea

SOURCE: Alimentary Pharmacology and Therapeutics (2003), 18(Suppl. 1), 45-54
CODEN: APTHEN; ISSN: 0269-2813

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

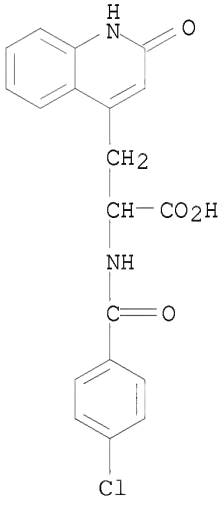
AB Helicobacter pylori infection elicits persistent neutrophil infiltration in gastric mucosa. The expression of cyclooxygenase (COX)-2 and

inhibition of apoptosis in the neutrophils could contribute to the pathogenesis of H. pylori infection. Rebamipide, a mucosal protective and ulcer-healing drug, has been known to inhibit neutrophil activation. The objective of this study was to evaluate the effect of rebamipide on the neutrophils activated by H. pylori water-soluble proteins. After neutrophils were stimulated with H. pylori water extract (HPWE) or pre-treated with rebamipide, the expression of COX-2 mRNA and protein was assessed by quant. RT-PCR and Western blotting, resp. Prostaglandin (PG) E2 synthesis was determined by RIA. Neutrophil apoptosis was evaluated by cytosolic oligonucleosome-bound DNA ELISA and caspase-3 activity was measured by the detection of p-nitroanilide after cleavage from labeled substrate. Stimulation with HPWE up-regulated COX-2 expression and PGE2 secretion, and inhibited neutrophil apoptosis. Rebamipide suppressed PGE2 secretion from neutrophils dose-dependently. Rebamipide, however, did not affect neutrophil apoptosis and caspase-3 activity. Thus, rebamipide effectively suppressed PGE2 secretion from neutrophils activated by H. pylori water-soluble proteins. This is another possible mechanism of gastric mucosal protection by rebamipide.

IT 90098-04-7, Rebamipide
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of rebamipide on the expression of proinflammatory mediators and apoptosis in human neutrophils by Helicobacter pylori water-soluble surface proteins)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



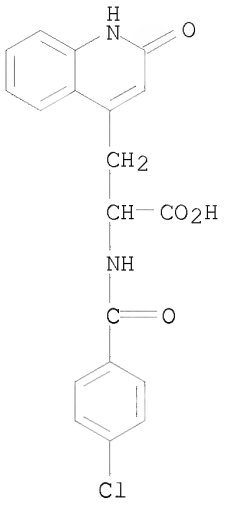
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 31 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 140:104220 CA

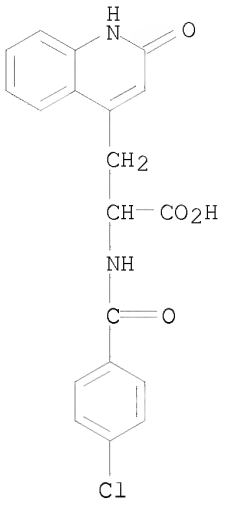
TITLE: Review article: clinical significance of mucosal-protective agents: acid, inflammation, carcinogenesis and rebamipide

AUTHOR(S): Haruma, K.; Ito, M.
CORPORATE SOURCE: Division of Gastroenterology, Department of Internal Medicine, Kawasaki Medical School, Kurashiki, 701-0192, Japan
SOURCE: Alimentary Pharmacology and Therapeutics (2003), 18(Suppl. 1), 153-159
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. While a great deal of clin. evidence has been found regarding anti-acids for the treatment of gastric disorders including peptic ulcers, not all disorders can be explained only by the hyperfunction of acid secretion. Especially in the Asian region, glandular atrophy is more prominent than in Western countries, therefore low acid output is often observed in these patients. Improvement of mucosal protection is rational therapy for these patients; this is the reason for use of these agents in Asian countries. Rebamipide has many biol. activities for gastric mucosa such as increasing the blood flow and biosynthesis of prostaglandins and the decrease of oxygen radicals. These suggest the possible efficacy of rebamipide in the prevention of both Helicobacter pylori-related and non-steroidal antiinflammatory drug (NSAID)-induced gastric injury, which has been proved by human studies. Rebamipide is the only mucosal-protective drug which can improve the histol. gastritis in vivo, whereas anti-acids have a lesser effect in influencing gastritis. Improvement of gastritis is expressed not only in quantity but also in quality of gastritis, which is shown as the reduction of NOS expression in the gastric mucosa. Clin., it is suggested that rebamipide has the potential to prevent gastric carcinogenesis by improvement of histol. gastritis.
IT 90098-04-7, Rebamipide
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clin. significance of mucosal-protective agents such as rebamipide for treating gastric inflammation and preventing carcinogenesis)
RN 90098-04-7 CA
CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 32 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 140:104219 CA
TITLE: Review article: rebamipide and the digestive epithelial barrier
AUTHOR(S): Matysiak-Budnik, T.; Heyman, M.; Megraud, F.
CORPORATE SOURCE: Faculte de Medecine Necker-Enfants Malades, INSERM EMI-0212, Paris, 75730, Fr.
SOURCE: Alimentary Pharmacology and Therapeutics (2003), 18(Suppl. 1), 55-62
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Rebamipide exerts a pos. effect on the digestive epithelial barrier by reinforcing its integrity in normal and in inflammatory conditions, and by normalizing the macromol. transport across this barrier, increased by Helicobacter infection. Moreover, in mice, rebamipide is capable of diminishing allergic sensitization and of counteracting the inhibitory effect of Helicobacter pylori on oral tolerance to dietary antigens. These properties of rebamipide could explain its antiinflammatory activity with respect to the digestive mucosa and could provide protection against allergic sensitization to foreign antigens in susceptible individuals.
IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of rebamipide on the digestive epithelial barrier and relevance for antiinflammatory activity and diminishing allergic sensitization to dietary antigens)
RN 90098-04-7 CA
CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)

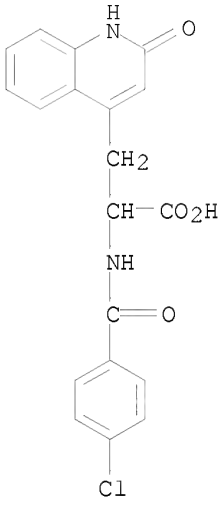


REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 33 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 140:104218 CA
TITLE: Review article: the role of rebamipide in the management of inflammatory disease of the gastrointestinal tract
AUTHOR(S): Genta, R. M.
CORPORATE SOURCE: Department of Pathology, University of Geneva, Switz.
SOURCE: Alimentary Pharmacology and Therapeutics (2003), 18(Suppl. 1), 8-13
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Rebamipide stimulates the generation of endogenous prostaglandins in the gastric mucosa and is reported to accelerate ulcer healing. This review discusses whether rebamipide can prevent Helicobacter pylori infection, reduce inflammation, accelerate healing after eradication, promote ulcer healing, and prevent progression of preneoplastic lesions. Furthermore, we evaluate its usefulness in other inflammatory conditions of the gastrointestinal tract. We conclude that rebamipide is an important candidate for long-term suppression of gastrointestinal inflammation, particularly if reducing the complications of H. pylori infection without eradicating the organism becomes accepted. If its ability to accelerate mucosal normalization is confirmed, rebamipide could be added to eradication regimens. Little information exists on whether such therapy could help limit the development of pre-neoplastic lesions. In light of the dearth of effective drugs to control inflammation in idiopathic inflammatory bowel disease, the potential of any promising new and safe compound deserves to be fully explored. The next step is to devise a targeted plan of translational research, so that results from the bench may be used to design rigorously controlled international clin. trials.

IT 90098-04-7, Rebamipide
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(role of rebamipide in the management of inflammatory disease of the gastrointestinal tract)
RN 90098-04-7 CA
CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

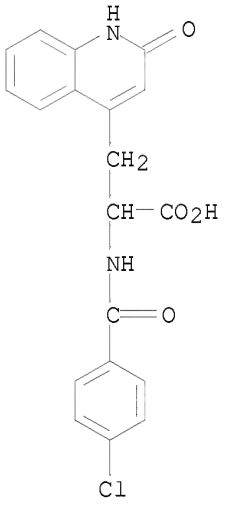
L15 ANSWER 34 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 140:87411 CA
TITLE: Inhibitory effect of rebamipide on the generation of acute gastric mucosal lesions in streptozotocin-induced diabetic rats
AUTHOR(S): Otsuka, Masahito; Kanazawa, Masao
CORPORATE SOURCE: The Third Department of Internal Medicine, Tokyo Medical University Hospital, Japan
SOURCE: Tokyo Ika Daigaku Zasshi (2003), 61(3), 274-280
CODEN: TIDZAH; ISSN: 0040-8905
PUBLISHER: Tokyo Ika Daigaku Igakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB It is known that acute gastric mucosal lesions (AGML) are frequently observed by 24-h fasting in rats with diabetes induced by i.p. injection of streptozotocin (STZ). We evaluated the effect of gastric acid and rebamipide, a free radical scavenger, on the generation of AGML in diabetic rats. The total amount of gastric acid secreted by diabetic rats during 60 min after i.p. administration of amogastrin at 120 mg/kg was significantly less than that secreted by control rats (0.8±0.6 mEq/L vs. 2.6±1.4 mEq/L, $p<0.01$). Serum gastrin level in diabetic rats was significantly higher than that in control rats, indicating that the decrease in gastric acid secretion was due to gastric mucosal dysfunction.

No AGML was observed by 24-h fasting (free water drinking) in diabetic rats with administration of rebamipide (n=15) at 100 mg/kg four times at 6-h intervals, while 50 % of diabetic rats without rebamipide (n=14) generated AGML under the same condition. The content of thiobarbituric acid reactants in the gastric mucosa in diabetic rats with administration of rebamipide was significantly less than that in diabetic rats without rebamipide (53.6±19.9 vs. 75.1±21.8 n mol./g w.w., $p<0.05$). Considering that rebamipide has a free radical scavenging effect, it is suggested that rebamipide may have prevented the occurrence of fasting-induced AGML in diabetic rats by decreasing free radical in gastric mucosa.

IT 90098-04-7, Rebamipide
RL: DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitory effect of rebamipide on the generation of acute gastric mucosal lesions in streptozotocin-induced diabetic rats)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



L15 ANSWER 35 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 140:70713 CA

TITLE: Inhibitory effects of famotidine on NSAIDs and bisphosphonate-induced gastric mucosal lesions in rats: Comparison with proton pump inhibitor and gastric mucosal protective agents

AUTHOR(S): Keto, Yoshihiro; Funatsu, Toshiyuki; Hirata, Takuya; Toyama, Takehiro; Sudoh, Katsumi; Sasamata, Masao

CORPORATE SOURCE: Applied Pharmacology Research, Pharmacology Laboratories, Institute for Drug Discovery Research, Yamanouchi Pharmaceutical Co., Ltd., Japan

SOURCE: Japanese Pharmacology & Therapeutics (2003), 31(6), 485-493
CODEN: JPTABU

PUBLISHER: Raifu Saiensu Shuppan K.K.

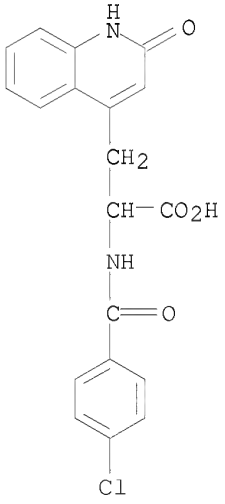
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB In the present study, we investigated the inhibitory effects of famotidine, omeprazole, rebamipide and teprenone on acute gastric mucosal lesions induced by NSAIDs (diclofenac and aspirin) or a bisphosphonate (alendronate) in rats. Famotidine (0.3, 1, 3 mg/kg), omeprazole (1, 3, 10mg/kg), rebamipide (10, 30 100 mg/kg) and teprenone (10, 30, 100 mg/kg) were orally administered with NSAIDs or alendronate 1 h after s.c. indomethacin (20 mg/kg) injection. Famotidine and omeprazole dose-dependently suppressed the drug-related gastric lesions. However, rebamipide (100 mg/kg) and teprenone (30 and 100 mg/kg) at the high dose suppressed the gastric mucosal lesion induced by alendronate but not by NSAIDs. Famotidine also markedly inhibited gastric acid secretion when administered at 1 or 3 h before pylorus ligation. Omeprazole significantly inhibited the gastric acid secretion only when administered at 3 h but not at 1 h before pylorus ligation. Neither rebamipide nor teprenone affected the gastric acid secretion at either administration time. These results suggest that the inhibitory effects of famotidine co-administered with NSAIDs or bisphosphonate on gastric mucosal damage are more potent than those of omeprazole, rebamipide and teprenone because only famotidine promptly inhibits gastric acid secretion. Thus, famotidine appears to be superior to omeprazole, rebamipide and teprenone in its usefulness to prevent NSAIDs and bisphosphonate-induced acute gastric mucosal lesions.

IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect; inhibitory effects of famotidine on NSAIDs and bisphosphonate-induced gastric mucosal lesions in rats and comparison with proton pump inhibitor and gastric mucosal protective agents)

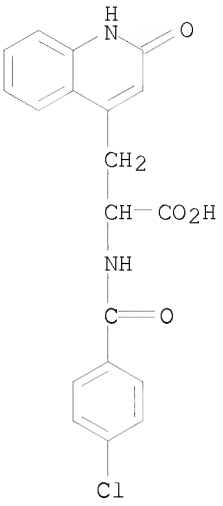
RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



L15 ANSWER 36 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 140:53105 CA
TITLE: Application of in vivo ESR spectroscopy to pharmaceutical sciences: evaluation of in vivo inhibitory mechanism of antigastric lesion drugs
AUTHOR(S): Kasazaki, K.; Yasukawa, K.; Sano, H.; Yamada, K.; Utsumi, H.
CORPORATE SOURCE: Department of Bio-function Analysis, Graduate School of Pharmaceutical Sciences, Kyushu University, Fukuoka, Japan
SOURCE: Applied Magnetic Resonance (2003), 23(3-4), 585-595
CODEN: APMREI; ISSN: 0937-9347
PUBLISHER: Springer-Verlag Wien
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In order to analyze free radical reactions in living stomach, the authors developed a noninvasive measurement by an in vivo ESR and spin probe technique and applied it to mucosal injury. NH4OH-induced gastric lesions were prepared in rats. A nitroxyl probe was administered intragastrically or i.v., and then in vivo ESR spectra of the gastric region were obtained by 300 MHz ESR spectroscopy. The signal of the intragastrically administered spin probe decreased gradually and the decay significantly enhanced 30 min after NH4OH administration. The enhanced signal decay was attributed to the OH radical generation, since it was completely suppressed by mannitol, catalase, and desferrioxamine. Two com. available antigastric lesion drugs, rebamipide and taurine, were tested with a NH4OH-induced gastric lesion model. Both i.p. administration of rebamipide and i.v. administration of taurine suppressed gastric lesion formation induced by NH4OH in a dose-dependent manner. I.p. preadministration of rebamipide also suppressed the enhanced signal decay, but neither pre- nor coadministration of taurine showed any effect on the enhanced signal decay. The results strongly indicate that the inhibitory mechanism on gastric lesion formation in NH4OH-treated rats is quite different for the 2 antigastric lesion drugs rebamipide and taurine.
IT 90098-04-7, Rebamipide
RL: DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ESR spectroscopic evaluation of in vivo inhibitory mechanism of antigastric lesion drugs)
RN 90098-04-7 CA
CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



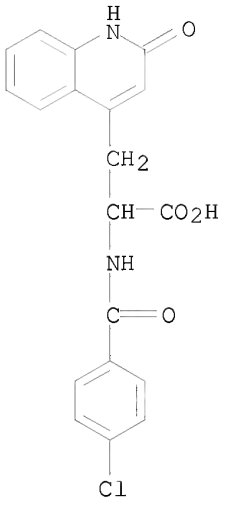
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 37 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 140:35876 CA
TITLE: Therapeutic effect of rebamipide in a modified acetic acid-induced buccal mucosal ulcer model
AUTHOR(S): Ishiyama, Hironobu; Kawai, Kazuyoshi; Azuma, Atsushi; Nagano, Chifumi
CORPORATE SOURCE: Third Institute of New Drug Discovery, Otsuka Pharmaceutical Co. Ltd., Kawauchi-cho, Tokushima, 771-0192, Japan
SOURCE: Inflammopharmacology (2002), 10(4-6), 391-399
CODEN: IAOAES; ISSN: 0925-4692
PUBLISHER: VSP BV
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Previous studies have suggested that rebamipide, a gastroprotective drug, might be effective for the treatment of aphthous oral ulcers in Behget's disease patients. The aim of this study was to confirm the effect of rebamipide on exptl. induced stomatitis in a rat acetic acid-induced oral ulcer, model. Buccal mucosal lesions were induced by local injection of 50 μl of 99.7% acetic acid into the buccal mucosa, which produced a single large ulcer in each of the treated rats. The ulcer remained up to 14 days. Repeated dose of rebamipide (3-100 mg/kg) dose-dependently decreased the ulcer area. Histopathol., increased fibrosis and regenerated epithelium were observed in the rebamipide-treated group. In contrast, indomethacin, a cyclooxygenase inhibitor, impaired the healing of ulcers. We have successfully established an improved method for the administration of acetic acid to induce oral ulcers, and rebamipide accelerated the ulcer healing.
IT 90098-04-7, Rebamipide
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(therapeutic effect of rebamipide in modified acetic acid-induced buccal mucosal ulcer model)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 38 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 139:391484 CA

TITLE: Gastric restitution is inhibited by dexamethasone, which is reversed by hepatocyte growth factor and rebamipide

AUTHOR(S): Takahashi, M.; Takada, H.; Takagi, K.; Kataoka, S.; Soma, R.; Kuwayama, H.

CORPORATE SOURCE: Department of Gastroenterology and Hepatology, University Hospital at Koshigaya, Dokkyo University School of Medicine, Saitama, 343-8555, Japan

SOURCE: Alimentary Pharmacology and Therapeutics (2003), 18(Suppl. 1), 126-132
CODEN: APTHEN; ISSN: 0269-2813

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

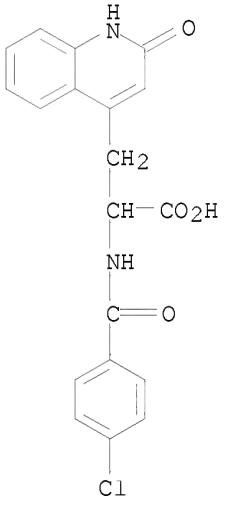
AB Background: Glucocorticoids have been shown to induce peptic ulcers, especially when co-administered with NSAIDs. Hepatocyte growth factor (HGF) plays a role in gastric ulcer repair, facilitating the restitution of gastric mucosal epithelial cells. HGF expression is induced by PGs in gastric fibroblasts. We hypothesized that dexamethasone (DEX) may inhibit PG production and HGF expression, thus inhibiting HGF-induced gastric epithelial restitution. Aim: To investigate the effect of DEX on gastric restitution, using cultured gastric cells, the role of HGF in the restitution inhibited by DEX, and the effect of rebamipide on DEX-inhibited restitution. Methods: Human gastric fibroblasts were prepared from human stomach obtained at surgery; PGE2 and HGF is determined by ELISA;

Restitution was assessed by the round wound restitution model, using coculture of gastric fibroblasts and epithelial cells; COX-2 and HGF mRNA were quantified by TaqMan RT-PCR system. Results: (1) DEX inhibited HGF mRNA and COX-2 mRNA, and accordingly inhibited PGE2 and HGF release. (2) DEX inhibited the restitution of gastric cells, which (3) was reversed by HGF and rebamipide to the same extent. (4) Rebamipide induced PGE2 and HGF. Conclusion: DEX inhibits restitution via HGF depletion, and rebamipide reverses the inhibited restitution by HGF induction.

IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dexamethasone inhibited gastric restitution and PGE2 release is reversed by HGF and rebamipide)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 39 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 139:390974 CA

TITLE: A cross-sectional retrospective assessment of anti-arthritic drugs in patients with arthritis in Korea

AUTHOR(S): Lee, Myung Chul; Lee, Seokhyun; Suh, Dong-Churl; Kim, Jeeyeon; Kong, Sheldon X.; Ahn, Jiwhan; Bae, Daekyung; Chae, Injung; Cho, Wooshin; Cho, YoonJae; Choi, Jangsuk; Han, Changdong; Hwang, Deuksoo; Hwang, Kuhnsung; Kim, Jungman; Kim, Sedong; Moon, Eunsun; Lee, Sooho; Park, Ilhyung; Park, Myungsik; Park, Yunsoo; Suh, Jeungtak; Sung, Sangcheol

CORPORATE SOURCE: Korea Arthritis Study Group, Seoul National University Hospital, Seoul, S. Korea

SOURCE: Current Medical Research and Opinion (2003), 19(7), 597-602

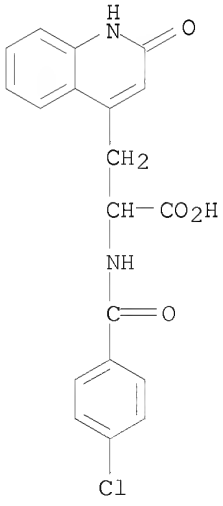
CODEN: CMROCX; ISSN: 0300-7995
PUBLISHER: LibraPharm Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: Selective cyclooxygenase-2 (COX-2) inhibitors were recently introduced for the treatment of arthritis because of their lower rates of gastrointestinal adverse events compared with traditional non-steroidal anti-inflammatory drugs (NSAIDs). Objective: To examine the medication usage patterns for both osteoarthritis (OA) and rheumatoid arthritis (RA) in Korea. Methods: The medical charts of a convenience sample of 402 patients with OA or RA were reviewed by the Arthritis Study Group in 14 hospitals and ten clinics in Korea. Results: Traditional oral NSAIDs were the most commonly prescribed drugs for OA (68.3%) and RA (65.1%) patients. Two-thirds (66.7%) of the RA patients taking COX-2 inhibitors were prescribed other arthritis medications concurrently and 85.1 of RA patients taking NSAIDs were prescribed other arthritis medications concurrently. Patients on NSAIDs were almost twice as likely to have a gastroprotective agent (GPA) concurrently compared to COX-2 inhibitor users (OA patients 38.1% vs. 21.2%; RA patients 57.9% vs. 30.6%). Overall, patients taking COX-2 inhibitors were less likely to take GPAs concurrently compared to patients not taking COX-2 inhibitors (unadjusted OR 0.36; adjusted OR 0.39). Conclusions: Traditional oral NSAIDs were commonly prescribed to arthritis patients in Korea. In this study, patients taking COX-2 inhibitors were prescribed less adjunctive arthritis treatments and less gastroprotective agents than traditional oral NSAID users.

IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cross-sectional retrospective assessment of antiarthritic drugs in Korean patients with arthritis)

RN 90098-04-7 CA

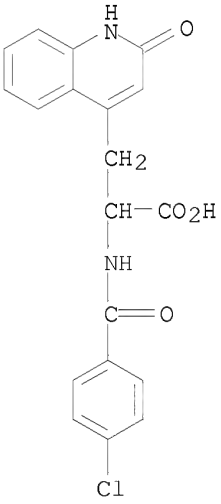
CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 40 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 139:354244 CA
TITLE: A stability study of a rebamipide enema: A hospital pharmaceutical preparation
AUTHOR(S): Hamamoto, Tomoyuki; Nakashima, Mikiro; Nakabo, Yukiko; Komine, Yoshio; Fukuchi, Hiromitsu; Ichikawa, Nobuhiro; Makiyama, Kazuya; Sasaki, Hitoshi
CORPORATE SOURCE: Dep. Hosp. Pharmacy, Nagasaki Univ. Sch. Med., Nagasaki, 852-8501, Japan
SOURCE: Nippon Byoin Yakuzaishikai Zasshi (2003), 39(9), 1155-1159
CODEN: NBYZEB; ISSN: 1341-8815
PUBLISHER: Nippon Byoin Yakuzaishikai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB A hospital pharmaceutical preparation, rebamipide (Mucosta) enema, was found to be stable in terms of appearance and pH, when stored for 4 wk under 1000-lx irradiation at 25° or in the dark at 25° or 10°, except that time-dependent particle preparation was observed Viscosity of the rebamipide preparation was unchanged only when kept in the dark at 10°. Viscosity of CM-cellulose Na, a base for the enema, was variable depending on storage conditions.
IT 90098-04-7, Mucosta
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stability study of hospital pharmaceutical preparation, rebamipide enema)
RN 90098-04-7 CA
CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



L15 ANSWER 41 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 139:306426 CA
TITLE: Gastric Helicobacter infection inhibits development of

oral tolerance to food antigens in mice

AUTHOR(S): Matysiak-Budnik, Tamara; van Niel, Guillaume; Megraud, Francis; Mayo, Kathryn; Bevilacqua, Claudia; Gaboriau-Routhiau, Valerie; Moreau, Marie-Christiane; Heyman, Martine

CORPORATE SOURCE: INSERM EMI-0212, Faculte de Medecine Necker-Enfants Malades, Paris, Fr.

SOURCE: Infection and Immunity (2003), 71(9), 5219-5224
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

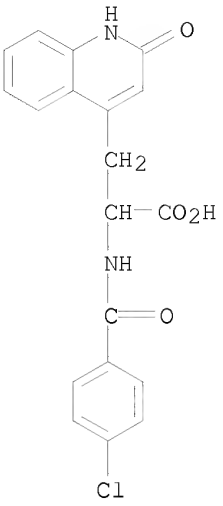
LANGUAGE: English

AB The increase in the transcellular passage of intact antigens across the digestive epithelium infected with Helicobacter pylori may interfere with the regulation of mucosal immune responses. The aim of this work was to study the capacity of Helicobacter infection to inhibit the development of oral tolerance or to promote allergic sensitization and the capacity of a gastro-protective agent, rebamipide, to interfere with these processes in mice. Oral tolerance to ovalbumin (OVA) was studied in 48 C3H/He 4-wk-old mice divided into four groups: (i) OVA-sensitized mice; (ii) OVA-"tolerized" mice (i.e., mice that were rendered immunol. tolerant); (iii) H. felis-infected, OVA-tolerized mice; and (iv) and H. felis-infected, OVA-tolerized, rebamipide-treated mice. Oral sensitization to hen egg lysozyme (HEL) was studied in 48 mice divided into four groups: (i) controls; (ii) HEL-sensitized mice; (iii) H. felis-infected, HEL-sensitized mice; and (iv) H. felis-infected, HEL-sensitized, rebamipide-treated mice. Specific anti-OVA or anti-HEL IgE and IgG1/IgG2a serum titers were measured by ELISA. Addnl., the capacity of rebamipide to interfere with antigen presentation and T-cell activation in vitro, as well as absorption of rebamipide across the epithelial monolayer, was tested. H. felis infection led to the inhibition of oral tolerance to OVA, but rebamipide prevented this inhibitive effect of H. felis. H. felis infection did not enhance the sensitization to HEL, but rebamipide inhibited the development of this sensitization. Moreover, rebamipide inhibited in a dose-dependent manner antigen presentation and T-cell activation in vitro and was shown to be able to cross the epithelium at a concentration capable of inducing this inhibitory effect. We conclude that H. felis can inhibit the development of oral tolerance to OVA in mice and that this inhibition is prevented by rebamipide.

IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gastric Helicobacter infection in altering oral tolerance to food antigens and effect of rebamipide)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

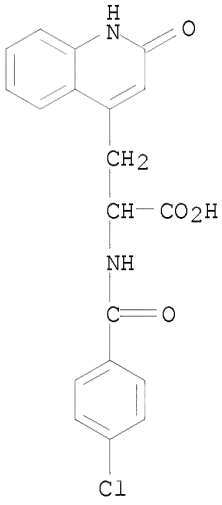
L15 ANSWER 42 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 139:255105 CA
TITLE: Effects of rebamipide, a gastro-protective drug on the Helicobacter pylori status and inflammation in the gastric mucosa of patients with gastric ulcer: a randomized double-blind placebo-controlled multicentre trial
AUTHOR(S): Fujioka, T.; Arakawa, T.; Shimoyama, T.; Yoshikawa, T.; Itoh, M.; Asaka, M.; Ishii, H.; Kuwayama, H.; Sato, R.; Kawai, S.; Takemoto, T.; Kobayashi, K.
CORPORATE SOURCE: Department of General Medicine, Oita Medical University, Oita, 879-5593, Japan
SOURCE: Alimentary Pharmacology and Therapeutics (2003), 18(Suppl. 1), 146-152
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Aims: To investigate the effects of rebamipide on the Helicobacter pylori eradication rate with amoxicillin and omeprazole. The trial also examined its histol. effects on gastro-mucosal inflammation after eradication. Methods: Two hundred and six H. pylori-pos. patients with active gastric ulcer underwent 8-wk based therapy (OA) consisting of 2-wk amoxicillin with omeprazole and subsequent 6-wk omeprazole. They randomly received either rebamipide (OA-R) or placebo (OA-P) for 16 wk: combined with the OA based therapy, and subsequently for another 8 wk. Besides eradication rate, inflammatory findings of gastric mucosa after eradication were evaluated histol. Results: Per Protocol Set anal. showed no significant difference in eradication rate between OA-R (64.6%; 95 %confidence interval, 54.3-75.0%) and OA-P (67.9%; 95% CI, 57.6-78.3%). Histol. findings in the gastric mucosa of the ulcer region, however, indicated a significant improvement (P = 0.017) in inflammation scores in OA-R (1.84

± 0.41) compared with that in OA-P (2.02 ± 0.39) after 16-wk of treatment. This suppressive effect on inflammation was observed even in the OA-R patients unsuccessfully eradicated. Conclusion: Rebamipide demonstrated a suppressive effect on the persistent and possibly chronic inflammation in the gastric mucosa of the ulcer region after eradication, but the drug did not improve the eradication rate.

IT 90098-04-7, Rebamipide
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of rebamipide, a gastro-protective drug on the Helicobacter pylori status and inflammation in the gastric mucosa of patients with gastric ulcer)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 43 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 139:254984 CA

TITLE: The specific expression of hypoxia inducible factor-1α in human gastric mucosa induced by nonsteroidal anti-inflammatory drugs

AUTHOR(S): Ito, M.; Tanaka, S.; Kim, S.; Kuwai, T.; Matsutani, N.; Kamada, T.; Kitadai, Y.; Sumii, M.; Yoshihara, M.; Haruma, K.; Chayama, K.

CORPORATE SOURCE: Department of Medicine and Molecular Science, Graduate School of Biomedical Science, Hiroshima University, Hiroshima, 734-8551, Japan

SOURCE: Alimentary Pharmacology and Therapeutics (2003), 18(Suppl. 1), 90-98
CODEN: APTHEN; ISSN: 0269-2813

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

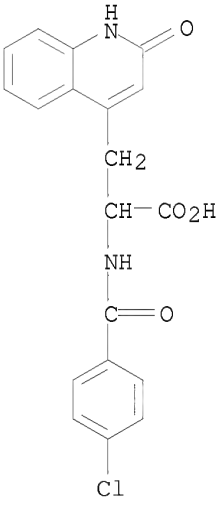
LANGUAGE: English

AB Background: Hypoxia is a cause of gastric mucosal damage induced by nonsteroidal anti-inflammatory drugs (NSAIDs). The expression of hypoxia inducible factor-1α (HIF-1α) reflects the status of tissue ischemia. Aim: To investigate the effect of NSAID administration on the expression of HIF-1α in human gastric mucosa. Methods: We employed 71 patients including 14 with NSAID administration. The HIF-1α expression was estimated by immunohistochem. using monoclonal antibody (H1α67) and raised antiserum (HI-3). Vascular endothelial growth factor expression was also examined by immunohistochem. HI-3 recognized hypoxia-induced protein in HeLa cells. Results: In human gastric mucosa, HIF-1α was mainly expressed in the nuclei of the surface epithelial cells and in the neck zone both by use of HI-3 and of H1α67. The expression of vascular endothelial growth factor correlated well with that of HIF-1α. The level of HIF-1α in the surface epithelium was significantly higher in patients with administration of NSAIDs than those without NSAID use ($P < 0.001$) both in the gastric corpus and antrum. Helicobacter pylori infection did not affected the levels of HIF-1α. Long-term administration of rebamipide reduced the level of HIF-1α. Conclusion: HIF-1α expression is a new biol. marker of ischemia especially in NSAID-related gastric lesions.

IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(specific expression of hypoxia inducible factor-1α in human gastric mucosa induced by nonsteroidal anti-inflammatory drugs)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 44 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 139:143669 CA

TITLE: Effects of polaprezinc on indomethacin-induced gastric antral ulcers in the refed rat: A comparison with

other cytoprotective anti-ulcer gents from the view of gastric mucosal protection

AUTHOR(S): Morita, Hitoshi; Ukawa, Hideki; Hori, Yuko; Miura, Naoyoshi; Yoneta, Tomoyuki; Kurimoto, Tadashi

CORPORATE SOURCE: Central Research Laboratories, ZERIA Pharmaceutical Co., Ltd., Japan

SOURCE: Japanese Pharmacology & Therapeutics (2002), 30(11), 949-954
CODEN: JPTABU

PUBLISHER: Raifu Saiensu Shuppan K.K.

DOCUMENT TYPE: Journal

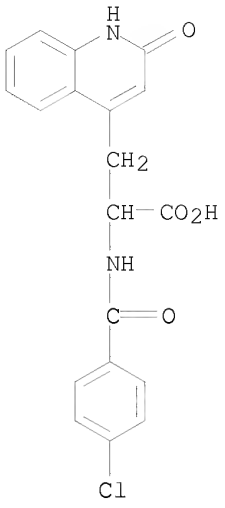
LANGUAGE: Japanese

AB The anti-ulcer agent polaprezinc is a chelate compound consisting of zinc ions and L-carnosine, that exhibits protective actions on the gastric mucosa without exerting antisecretory activity. We investigated the protective effects of polaprezinc and other cytoprotective anti-ulcer agents against indomethacin-induced gastric antral ulcers in the refed rat. Furthermore, we examined the effects of indomethacin pretreatment on the protective effects of these agents against acidified-ethanol-induced gastric lesions, to elucidate their mechanism of action. S.c. indomethacin (30 mg/kg) injection was administered to induce gastric antral ulcer formation in refed rats. Polaprezinc (1-10 mg/kg, p.o.) attenuated the progression of the indomethacin-induced ulcers in a dose-dependent manner. Although 16,16-dimetyl prostaglandin E2 (0.005 mg/kg, p.o.) also attenuated progression of the indomethacin-induced ulcers, ecabet-Na (10-100 mg/kg, p.o.), teprenone (10-100 mg/kg, p.o.) and rebamipide (10-100 mg/kg, p.o.) did not exert this effect. While the protective effects of polaprezinc and 16, 16-dimetyl prostaglandin E2 against acidified-ethanol-induced gastric lesions remained unaffected, those of ecabet-Na, teprenone and rebamipide were reduced following indomethacin pretreatment (5 mg/kg, s.c.). These results suggest that the protective effects of polaprezinc against the progression of indomethacin-induced gastric antral ulcers in the refed rat is independent of the involvement of endogenous prostaglandins. Thus, polaprezinc, like prostaglandin analogs, may also have therapeutic potential against gastric mucosal damage induced by non-steroidal anti-inflammatory drugs.

IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of polaprezinc on indomethacin-induced gastric antral ulcers in the refed rat, a comparison with other cytoprotective anti-ulcer gents from the view of gastric mucosal protection)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



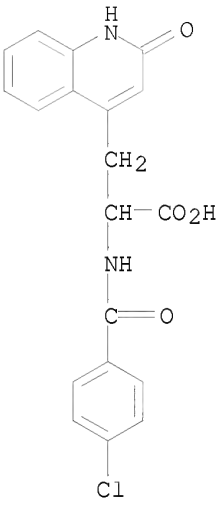
L15 ANSWER 45 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 139:143378 CA
TITLE: Combinatorial use of sodium laurate with taurine or L-glutamine enhances colonic absorption of rebamipide, poorly absorbable antiulcer drug, without any serious histopathological mucosal damages
AUTHOR(S): Miyake, Masateru; Oka, Yoshikazu; Minami, Takanori; Toguchi, Hajime; Odomi, Masaaki; Ogawara, Ken-Ichi; Higaki, Kazutaka; Kimura, Toshikiro
CORPORATE SOURCE: Department of Pharmaceutics, Faculty of Pharmaceutical Sciences, Okayama University, Okayama, 700-8530, Japan
SOURCE: Journal of Pharmaceutical Sciences (2003), 92(4), 911-921
CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors previously reported that the combinatorial use of sodium laurate (C12) with several amino acids such as taurine (Tau) and L-glutamine (L-Gln) enhanced the colonic absorption of phenol red with attenuating the local toxicity caused by C12. However, even these amino acids could not protect epithelial cells from being damaged if the mucosal damage got worse to the coagulation necrosis by an excessive dose of C12. Comparing C12 with sodium caprate (C10), used in drug products marketed, 100 μmol C10 was needed to exert the similar absorption-enhancement of rebamipide, a poorly absorbable antiulcer drug, to that by 10 μmol C12, and 100 μmol C10 was obviously more toxic to the mucosa than 10 μmol C12. The combinatorial use of C12 with Tau or L-Gln enhanced the colonic absorption of rebamipide 4-9 times larger in AUC than the control. Histopathol. studies clearly showed that Tau and L-Gln exerted the cytoprotective action on epithelial cells suffering from slight damages such as shrinkage and exfoliation, more articulately at 6 h than at 1.5 h after dosing. In conclusion, the combinatorial use of C12 with Tau or L-Gln could lead to a novel formulation improving the bioavailability of

poorly absorbable drugs without any serious local damages.

IT 90098-04-7, Rebamipide
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sodium laurate with taurine or L-glutamine enhances colonic absorption of rebamipide without histopathol. mucosal damages)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 46 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 139:127302 CA

TITLE: Determination of rebamipide in plasma by high performance liquid chromatography

AUTHOR(S): Zu, Luning; Li, Li; Yu, Dahai

CORPORATE SOURCE: The 404th Hospital of PLA, Weihai, 264200, Peop. Rep. China

SOURCE: Zhongguo Yiyuan Yaoxue Zazhi (2002), 22(6), 353-355
CODEN: ZYYAEP; ISSN: 1001-5213

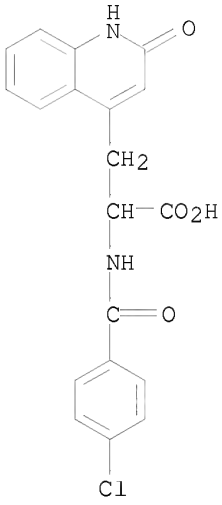
PUBLISHER: Zhongguo Yiyuan Yaoxue Zazhi Bianjibu

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB A HPLC method was established to determine rebamipide in plasma. The concentration of the drug was determined within 10 min by the method on a column of Kromasil C18 with MeOH-K dihydrogen phosphate (55:45, pH 3.0) as mobile phase and the detection at 230 nm. The rebamipide concns. in plasma were determined following a single oral dose of 600 mg. Good linear relation between concentration in plasma and peak area at 10-1200 μg mL-1 was obtained. Good precision and reproducibility were found. The relative and absolute average recoveries were (97.5 ±0.51)% and (90.3 ± 1.78)% (n 5), resp. The detection limit was 2 μg mL-1. The method was suitable for the determination

of rebamipide in body fluids.
IT 90098-04-7, Rebamipide
RL: ANT (Analyte); ANST (Analytical study)
(determination of rebamipide in plasma by high performance liquid chromatog.)
RN 90098-04-7 CA
CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



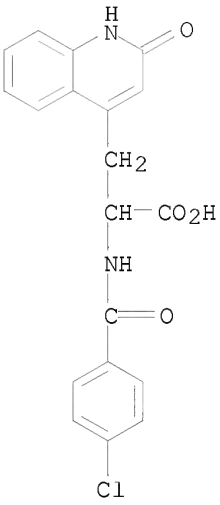
L15 ANSWER 47 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 139:95166 CA
TITLE: Characteristics of attenuating effects of rebamipide, an anti-ulcer agent, on oxidative burst of human neutrophils
AUTHOR(S): Shimoyama, Tadashi; Fukuda, Shinsaku; Liu, Qiang; Fukuda, Yoshihiro; Nakaji, Shigeyuki; Sugawara, Kazuo
CORPORATE SOURCE: First Department of Internal Medicine, Hirosaki University School of Medicine, Hirosaki, 036-8562, Japan
SOURCE: Journal of Pharmacological Sciences (Tokyo, Japan) (2003), 91(2), 153-157
CODEN: JPSTGJ; ISSN: 1347-8613
PUBLISHER: Japanese Pharmacological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of this study was to characterize the effects of rebamipide on the oxidative burst of human neutrophils. The neutrophil oxidative burst was measured in the presence of rebamipide and cimetidine using lucigenin- or luminol-dependent chemiluminescence (LgCL or LmCL). Rebamipide inhibited the LmCL response stimulated with opsonized zymosan, 12-myristate 13-acetate phorbol, and calcium ionophore in a dose-dependent manner, but the LgCL response was inhibited when neutrophils were stimulated with opsonized zymosan. LmCL response was also dose-dependently attenuated by rebamipide even in the presence of cimetidine. Thus, addition of rebamipide to H2-receptor antagonists can be considered for the treatment of gastric

mucosal injury associated with oxidative stress.

IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(attenuating effects of rebamipide and cimetidine on oxidative burst of human neutrophils)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 48 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 139:46185 CA

TITLE: Chemoprevention of Helicobacter pylori-associated gastric carcinogenesis in a mouse model; is it possible?

AUTHOR(S): Hahm, Ki Baik; Song, Young Joon; Oh, Tae Young; Lee, Jeong Sang; Surh, Young-Joon; Kim, Young Bae; Yoo, Byung Moo; Kim, Jin Hong; Han, Sang Uk; Nahm, Ki Taik; Kim, Myung-Wook; Kim, Dae Yong; Cho, Sung Won

CORPORATE SOURCE: Genomic Research Center for Gastroenterology, Ajou Helicobacter Research Group, Ajou University School of Medicine, Suwon, S. Korea

SOURCE: Journal of Biochemistry and Molecular Biology (2003), 36(1), 82-94
CODEN: JBMBE5; ISSN: 1225-8687

PUBLISHER: Biochemical Society of the Republic of Korea

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

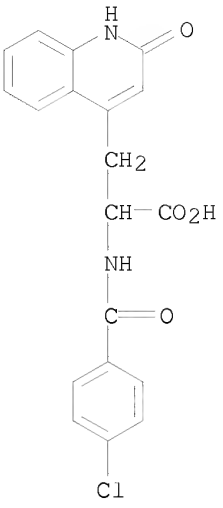
AB A review. Although debates still exist whether Helicobacter pylori infection is really class I carcinogen or not, H. pylori has been known to provoke precancerous lesions like gastric adenoma and chronic atrophic gastritis with intestinal metaplasia as well as gastric cancer. Chronic persistent, uncontrolled gastric inflammations are possible basis for

ensuing gastric carcinogenesis and H. pylori infection increased COX-2 expressions, which might be the one of the mechanisms leading to gastric cancer. To know the implication of long-term treatment of antiinflammatory drugs, rebamipide or nimesulide, on H. pylori-associated gastric carcinogenesis, we infected C57BL/6 mice with H. pylori, especially after MNU administration to promote carcinogenesis and the effects of the long-term administration of rebamipide or nimesulide were evaluated. C57BL/6 mice were sacrificed 50 wk after H. pylori infection. Colonization rates of H. pylori, degree of gastric inflammation and other pathol. changes including atrophic gastritis and metaplasia, serum levels and mRNA transcripts of various mouse cytokines and chemokines, and NF-κB binding activities, and finally the presence of gastric adenocarcinoma were compared between H. pylori infected group (HP), and H. pylori infected group administered with long-term rebamipide containing pellet diets (HPR) or nimesulide mixed pellets (HPN). Gastric mucosal expressions of ICAM-1, HCAM, MMP, and transcriptional regulations of NF-κB binding were all significantly decreased in HPR group than in HP group. Multi-probe RNase protection assay showed the significantly decreased mRNA levels of apoptosis related genes and various cytokines genes like IFN-γ, RANTES, TNF-α, TNFR p75, IL-1β in HPR group. In the experiment designed to provoke gastric cancer through MNU treatment with H. pylori infection, the incidence of gastric carcinoma was not changed between HP and HPR group, but significantly decreased in HPN group, suggesting the chemoprevention of H. pylori-associated gastric carcinogenesis by COX-2 inhibition. Long-term administration of antiinflammatory drugs should be considered in the treatment of H. pylori since they showed the mol. and biol. advantages with possible chemopreventive effect against H. pylori-associated gastric carcinogenesis. If the final concrete proof showing the causal relationship between H. pylori infection and gastric carcinogenesis could be obtained, that will shed new light on chemoprevention of gastric cancer, i.e., that gastric cancer could be prevented through either the eradication of H. pylori or lessening the inflammation provoked by H. pylori infection in high risk group.

IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemoprevention of Helicobacter pylori-associated gastric carcinogenesis in a mouse model)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 49 OF 220 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 139:26467 CA
TITLE: Bioequivalence of Rebamide tablets to Mucosta tablets (rebamipide 100 mg)
AUTHOR(S): Cho, Hea-Young; Jeong, Hyun-Cheol; Oh, Injoon; Moon, Jai-Dong; Lee, Yong-Bok
CORPORATE SOURCE: College of Pharmacy and Research Institute of Drug Development, Chonnam National University, Kwangju, 500-757, S. Korea
SOURCE: Yakche Hakhoechi (2001), 31(4), 281-287
CODEN: YAHAEX; ISSN: 0259-2347
PUBLISHER: Korean Society of Pharmaceutics
DOCUMENT TYPE: Journal
LANGUAGE: Korean

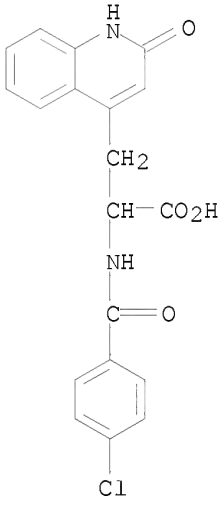
AB Rebamipide is a novel anti-gastric ulcer agent that has been reported to increase the synthesis of mucus, to increase the mucosal concentration of prostaglandin, and to promote rapid ulcer healing. The purpose of the present study was to evaluate the bioequivalence of two rebamipide tablets, Mucosta (Otsuka Korea Pharmaceutical Co., Ltd.) and Rebamide (Kyung Dong Pharmaceutical Co., Ltd.), according to the guidelines of Korea Food and Drug Administration (KFDA). The rebamipide release from the two rebamipide tablets in vitro was tested using KP VII Apparatus II method at pH 6.8 dissoln. media. Twenty normal male volunteers, 24.20 ± 2.26 yr in age and 66.19 ± 9.41 kg in body weight, were divided into two groups and a randomized 2 + 2 cross-over study was employed. After one tablet containing 100 mg of rebamipide was orally administered, blood was taken at predetd. time intervals and the concns. of rebamipide in serum were determined using HPLC method with fluorescence detector. The dissoln. profiles of two rebamipide tablets were very similar at pH 6.8 dissoln. media. Besides, the pharmacokinetic parameters such as AUCt, Cmax and Tmax were calculated and ANOVA test was utilized for the statistical anal. of the parameters. The results showed that the differences in AUCt, Cmax and

Tmax between two tablets based on the Mucosta were -2.57%, 5.77% and -1.47%, resp. Min. detectable differences (Δ) at α=0.05 and 1-β=0.8 were less than 20% (e.g., 12.62% and 17.63% for AUCt and Cmax, resp.). The powers (1-β) at α=0.05, Δ=0.2 for AUCt and Cmax were above 99.00% and 88.56%, resp. The 90% confidence intervals were within ± 20% (e.g., -9.96.apprx.4.82 and -4.54.apprx.16.09 for AUCt and Cmax, resp.). Two parameters met the criteria of KFDA for bioequivalence, indicating that Rebamide tablet is bioequivalent to Mucosta tablet.

IT 90098-04-7, Rebamipide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioequivalence of Rebamide tablets to Mucosta tablets containing rebamipide)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



L15 ANSWER 50 OF 220 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 138:362440 CA

TITLE: Efficacy of rebamipide as adjunctive therapy in the treatment of recurrent oral aphthous ulcers in patients with Behcet's disease: a randomised, double-blind, placebo-controlled study

AUTHOR(S): Matsuda, Takahide; Ohno, Shigeaki; Hirohata, Shunsei; Miyanaga, Yoshitaka; Ujihara, Hiroshi; Inaba, Goro; Nakamura, Satoshi; Tanaka, Shun-Ichi; Kogure, Mitsuko; Mizushima, Yutaka

CORPORATE SOURCE: Institute of Medical Science, St Marianna University School of Medicine, Kawasaki, Japan

SOURCE: Drugs in R&D (2003), 4(1), 19-28
CODEN: DRDDFD; ISSN: 1174-5886

PUBLISHER: Adis International Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

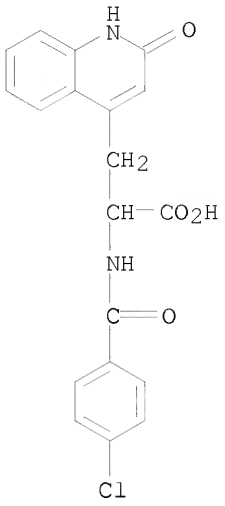
AB Background: Behcet's disease (BD) is a recurrent inflammatory disease

involving chronic recurrent oral aphthous ulcers (aphthae), uveitis, skin lesions and genital ulcers. We prospectively investigated the efficacy of rebamipide, a gastro-protective drug, against oral aphthous ulcers in BD patients. Methods: In a multicenter, double-blind, placebo-controlled study, 35 patients with BD, having as the main symptom oral aphthosis, were randomized to receive rebamipide 300 mg/day or placebo for 12 to 24 wk between August 1994 and Dec. 1996. Oral aphthosis must have occurred within 4 wk prior to enrollment and must have been visible for at least 7 days during that time. Oral aphthae count and pain scores were recorded daily in a diary by the patients themselves. Monthly aphthae count and pain scores were defined as the sum of aphthae count and pain scores for a month, resp. Investigators rated the global improvement in aphthae count and pain using a 6-point scale. The rate of change in monthly aphthae count and pain scores in the first 3 and last 3 mo of treatment were assessed in patients with more severe symptoms whose aphthae count and pain score were >28 at baseline (trial entry). Results: The rate of moderate or marked improvement in aphthae count and pain was 36% (5 of 14 subjects) in the placebo group and 65% (11 of 17 subjects) in the rebamipide group. During months 2 to 6 of treatment, aphthae count tended to increase and reached a peak at month 4 in the placebo group but decreased in the rebamipide group. Pain score decreased to the same extent in both groups for the first 3 mo of treatment; however, in the fourth to sixth months of treatment, the pain score tended to increase in the placebo group but decreased in the rebamipide group. In patients with a monthly aphthae pain score >28 at baseline, pain and count scores decreased throughout the 6 mo of rebamipide treatment but increased during the last 3 mo of treatment in the placebo group ($p < 0.01$ for the between-group comparisons). Conclusions: Rebamipide is well tolerated and improves the aphthae count and pain score in BD patients. It may therefore be useful in the treatment and prevention of frequently recurrent oral aphthous ulcers (not restricted to BD). Administration of rebamipide is not cumbersome, and it does not cause any discomfort, which corticosteroid ointments for example may do; furthermore, there are no specific adverse drug reactions. Rebamipide is therefore recommended as a long-term treatment for recurrent oral aphthous ulcers.

IT 90098-04-7, Rebamipide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy of rebamipide as adjunctive therapy in the treatment of recurrent oral aphthous ulcers in patients with Behcet's disease)

RN 90098-04-7 CA

CN 4-Quinolinepropanoic acid, α-[(4-chlorobenzoyl)amino]-1,2-dihydro-2-oxo- (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L2             0 S L1 SAM
L3             3 S L1 FULL
L4               STRUCTURE UPLOADED
L5             3 S L4 SAM
L6            61 S L4 FULL

     FILE 'CA' ENTERED AT 12:23:02 ON 23 JUL 2009
L7           349 S L6

     FILE 'REGISTRY' ENTERED AT 12:23:20 ON 23 JUL 2009
L8               STRUCTURE UPLOADED
L9             2 S L8 SAM
L10            0 S L8  SUB=L3 FULL
L11           48 S L8 FULL

     FILE 'CA' ENTERED AT 12:27:59 ON 23 JUL 2009
L12          347 S L11
L13          234 S L12 AND PY<2005
L14           14 S L13 AND CARBOSTYRIL
L15          220 S L13 NOT L14

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---Logging off of STN---
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Executing the logoff script...

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STN INTERNATIONAL LOGOFF AT 12:29:20 ON 23 JUL 2009